Synthesis and Reactions of bis(2,2,2-Trifluoroethyl)-β-Ketophosphonates

by

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ABSTRACT

The research contained herein is focused on a previously unreported synthesis of bis(2,2,2-trifluoroethoxy)-β-ketophosphonates *via* the hydration of the corresponding bis(2,2,2-trifluoroethoxy) alkynylphosphonates. The first step was to prepare all starting materials, namely the bis(2,2,2-trifluoroethyl) alkynylphosphonates from the corresponding commercially available terminal alkynes and bis(2,2,2-trifluoethoxy) phosphorochloridate. The hydration of the bis(2,2,2-trifluoroethoxy) alkynylphosphonates to yield the desired products was accomplished using mercury sulfate and 10% sulfuric acid. 2,2,2-Trifluoethanol was used as the solvent. The use of these β-keto phosphonates in the Horner-Wadsworth-Emmons reaction was also examined.

ACKNOWLEGEMENTS

I would like to thank Dr. John Jackson for giving me this project and for all of his guidance and direction in carrying it out. I would also like to thank Dr. Peter Norris and Dr. Howard Mettee for their feedback and all of their contributions as committee members on this project. I would like to express my gratitude towards Ray Hoff and Dr. Matthias Zeller for their computer and technical expertise, and for never being too busy to help me when I needed it. I am also grateful to the Department of Chemistry at Youngstown State University for this invaluable experience. I would also like to thank my parents for their support while pursuing the accomplishment of this academic and professional endeavor.

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LIST OF ABBREVIATIONS

Abreviation	Description
d	doublet
dt	doublet of triplets
dq	doublet of quartets
Et	ethyl
g	gram
GC	gas chromatography
HMPA	hexamethyl phosphoramide
Hz	Hertz
i-Pr	isopropyl
KHMDS	potassium hexamethyldisilazide
$KN(TMS)_2$	potassium hexamethyldisilazide
LHMDS	lithium hexamethyldisilazide
Me	methyl
MHz	megahertz
mL	milliliter
mmol	millimole
n-BuLi	*n*-butyllithium
NMR	nuclear magnetic resonance
Ph	Phenyl
ppm	parts per million

s	singlet
THF	tetrahydrofuran
TFE	trifluoroethyl
TLC	thin layer chromatography
TMS	tetramethylsilane

Chapter 1: Introduction

Background

Phosphonate compounds are diesters of pentavalent phosphorus and they are characterized by the structural composition depicted below (Figure 1):

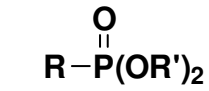


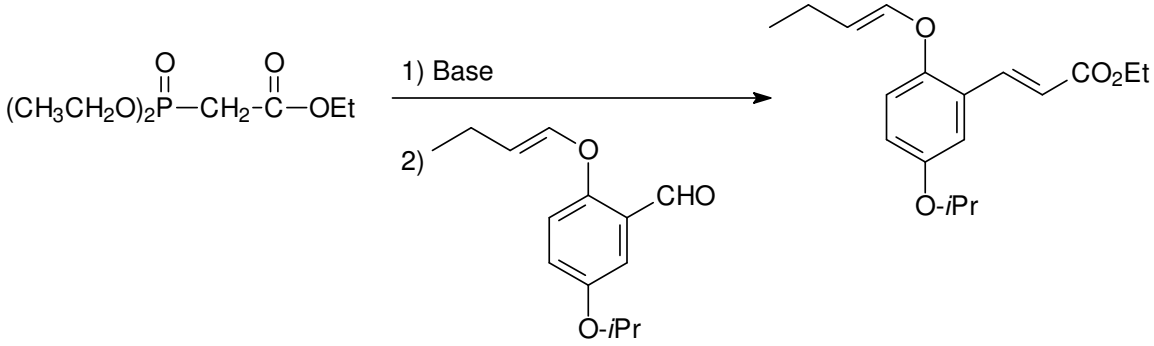
Figure 1: Chemical structure of phosphonates

Phosphonates were first synthesized in 1897 by Von Baeyer and Hoffman.[1] Since that time their properties have been extensively investigated, and recently phosphonates have been shown to have extensive potential as biological agents. Phosphonates may serve as pro-drugs[2] and nucleotide analogues of phosphonates may serve as antiviral agents [3] thus appearing to be useful in biochemistry and medicinal chemistry. Phosphonate compounds also have shown clinical promise as inhibitors of phosphate transport. Therefore, they may be potentially useful clinically in the treatment of conditions such as chronic renal insufficiency.[4] Because of their reactivity at phosphorus and the potential to be highly diversified in their chemical structure, phosphonates lend themselves to the synthetic organic chemist as useful synthetic intermediates.

Phosphonates as synthetic intermediates

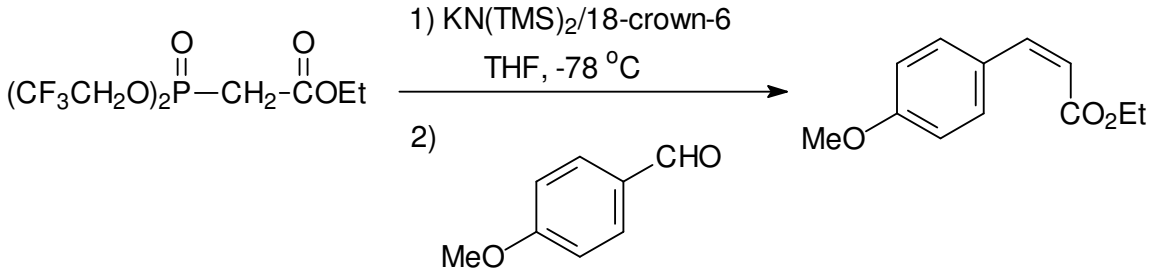
Phosphonates have great utility in synthetic organic chemistry. Their potential to incorporate many functional groups into their structure and the reactivity at phosphorus potentially allows them to undergo an enormous number of transformations.[5] The most popular reaction utilizing phosphonates as reagents is the Horner-Wadsworth–Emmons

reaction (HWE) to prepare α,β-unsaturated carbonyl compounds *via* their condensation with aldehydes. Under classic conditions if the ester portions of the phosphonate are simple alkoxy groups such as ethoxy or methoxy the more stable thermodynamic product, the (*E*)-isomer of the corresponding alkene is formed. An example is depicted (Scheme 1).



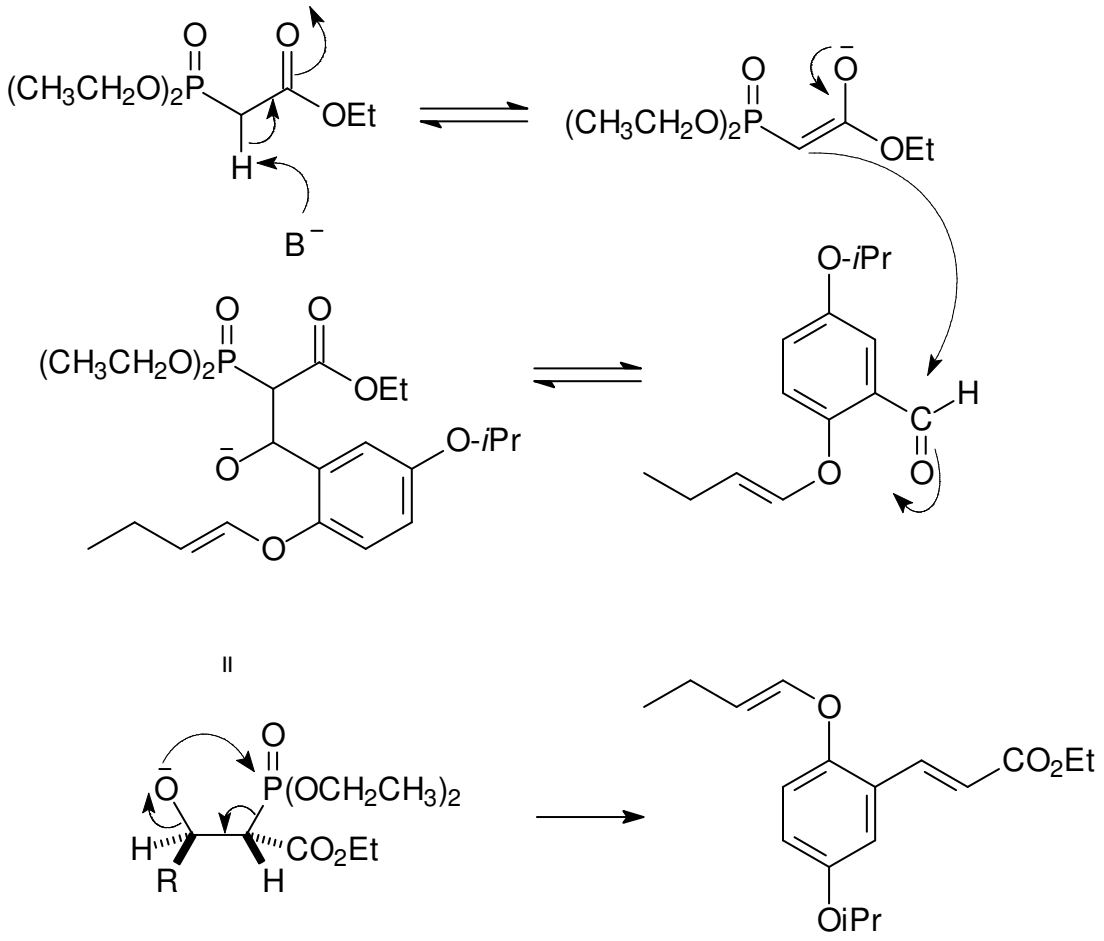
Scheme 1: Example of a typical Horner-Wadsworth-Emmons reaction.[35]

W. C. Still and C. Gennari have shown that the kinetic product, the (*Z*)-isomer of the corresponding alkene, predominates if electron-withdrawing groups such as bis(2,2,2-trifluoroethoxy) are substituted for the simple bis alkoxy moieties.[15, 16] This variation on the HWE is commonly referred to as the Still-Gennari HWE olefination and often uses strongly dissociated base systems such as potassium hexamethydisilazide [$KN(TMS)_2$] (also referred to as KHMDS) and 18-crown-6 ether (Scheme 2).

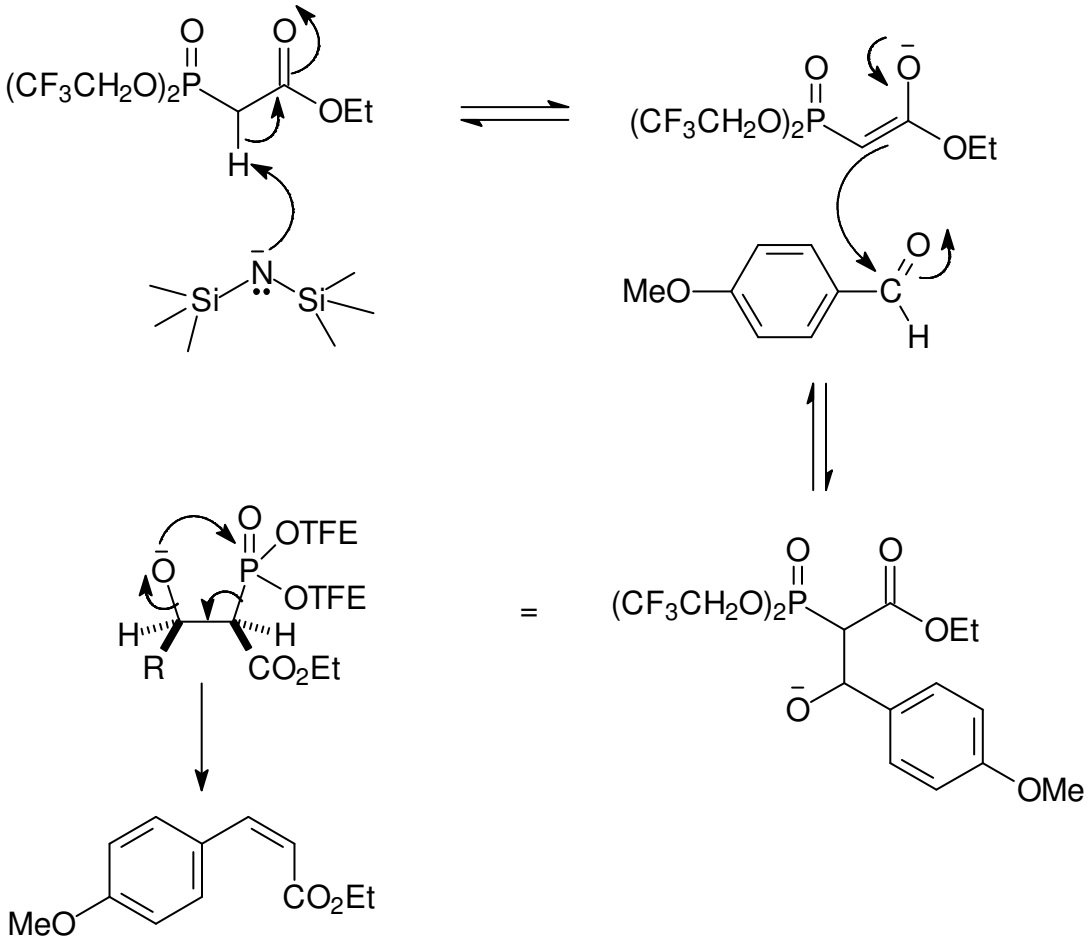


Scheme 2: Still-Gennari HWE olefination.[16]

The mechanisms for the formation of the thermodynamic product (*E*-isomer) and the kinetic adduct (*Z*-isomer) are illustrated respectively (Scheme 3 and Scheme 4):



Scheme 3: Mechanism for the formation of the thermodynamic (*E*)-isomer.[35]

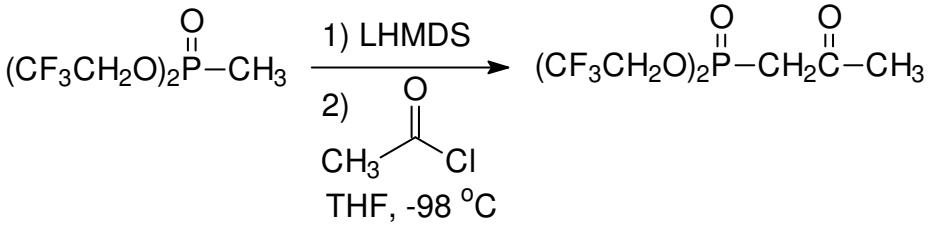


Scheme 4: Mechanism for the formation of the kinetic (*Z*)-isomer.[35]

Bis(2,2,2-trifluoroethyl)-β-ketophosphonates

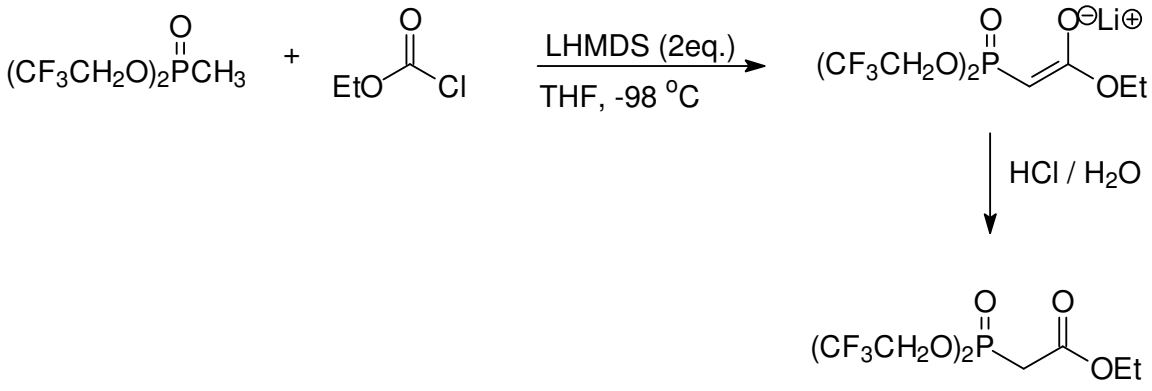
It has been brought to our attention through a recent SciFinder Scholar substructure search that there have only been 11 journal references and 5 patents containing either the preparations or attempted preparations of 14 different products that contain the fragment $(CF_3CH_2O)_2P(O)CR_2C(O)R$. The most common synthetic routes utilize the *in situ* formation of a lithium-stabilized anion from the treatment of the commercially available bis(2,2,2-trifluoroethyl) methylphosphonate with the strong base

lithium hexamethyldisilazide (LHMDS) in anhydrous THF at -98 °C. The subsequently formed carbanion nucleophile is then allowed to act upon an acid chloride to yield the respective β-ketophosphonate in good yields.[6-15] It has been reported that -98 °C is essential because the phosphonate carbanion decomposes at -78 °C.[15] A typical reaction scheme for the reported synthesis of bis(2,2,2-trifluoroethyl) β-ketophosphonates is illustrated (Scheme 5).



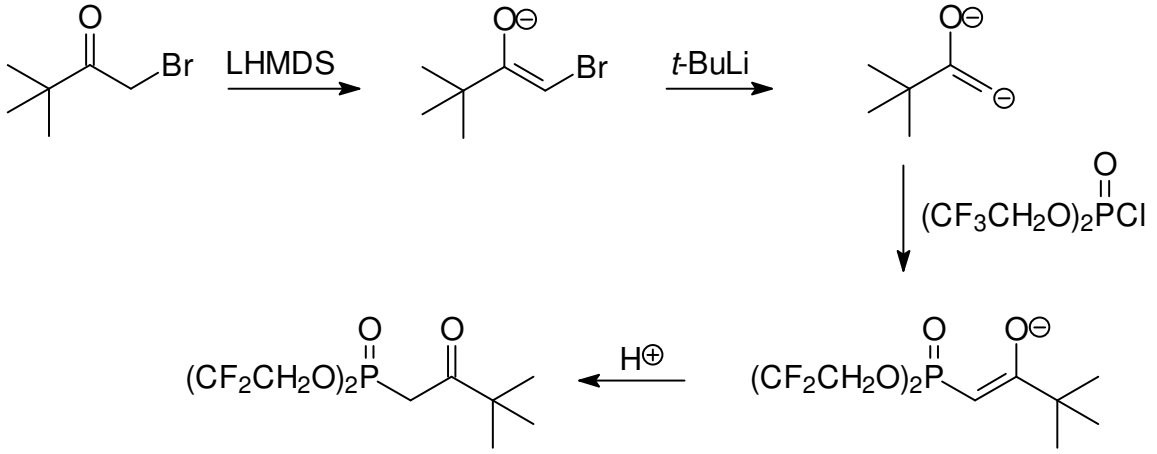
Scheme 5: Synthesis of a bis(2,2,2-trifluoroethyl)-β-ketophosphonate.

This method is based on the method reported by Savignac for the synthesis of bis(2,2,2-trifluoroethyl) phosphonoacetates from bis(2,2,2-trifluoroethyl) alkylphosphonates and alkylchloroformates utilizing LHMDS as the base and anhydrous THF as the solvent[17] (Scheme 6).



Scheme 6: Savignac's synthesis of bis(2,2,2-trifluoroethyl) phosphonoacetates.

Another strategy entails sequential treatment of an α-bromo ketone with lithium hexamethyldisilazide (LHMDS) followed by treatment with *tert*-butyllithium at -110 ^{o}C to form the dianion. The dianion nucleophile then acts upon the bis(2,2,2,-trifluorethyl) phosphorochloridate electrophile to prepare a limited number of bis(2,2,2-trifluoroethyl)-β-ketophosphonates in moderate to good yields[18] (Scheme 7).

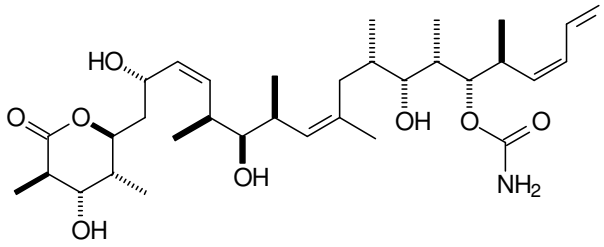


Scheme7: Wiemer synthesis of a bis(2,2,2-trifluoroethyl)-β-ketophosphonate.[18]

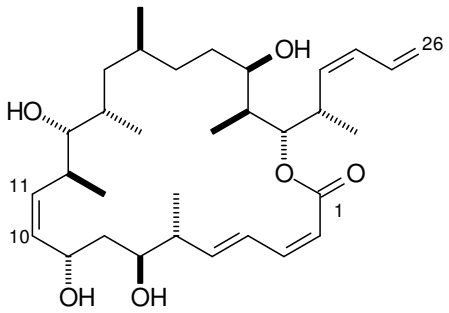
There has been considerable effort directed at natural product synthesis and significant progress has been made in the total synthesis of natural products in the recent years. Often natural products with interesting and useful properties are identified, but obtaining substantial quantities of them or their analogues is either not possible or prudent, thus making total synthesis the only way of obtaining useful quantities. Specifically the class of compounds known as antimitotic agents has received considerable attention. Paclitaxel, also known by the trade name Taxol®, was first isolated from the pacific yew tree which is native to the Pacific Northwestern United

States. Currenty Taxol® is widely prescribed as a chemotherapeutic agent, and it is an example of an antimitotic agent.

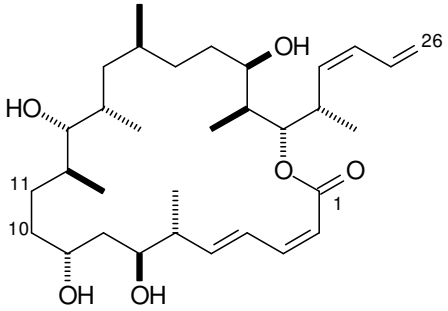
Antimitotic agents are known to promote formation and stabilization of microtubules; therefore, these classes of compounds holds promise as chemotherapeutic agents.[25-28] Other members of this family of compounds include (+)-discodermolide and (-)-dictyostatin. Both of these compounds were first isolated from deep sea sponge. 10,11-dihydrodictyostatin is an antimitotic analogue of dictyostatin. The chemical structures of these compounds are depicted below (Figure 2).



(+)-Discodermolide



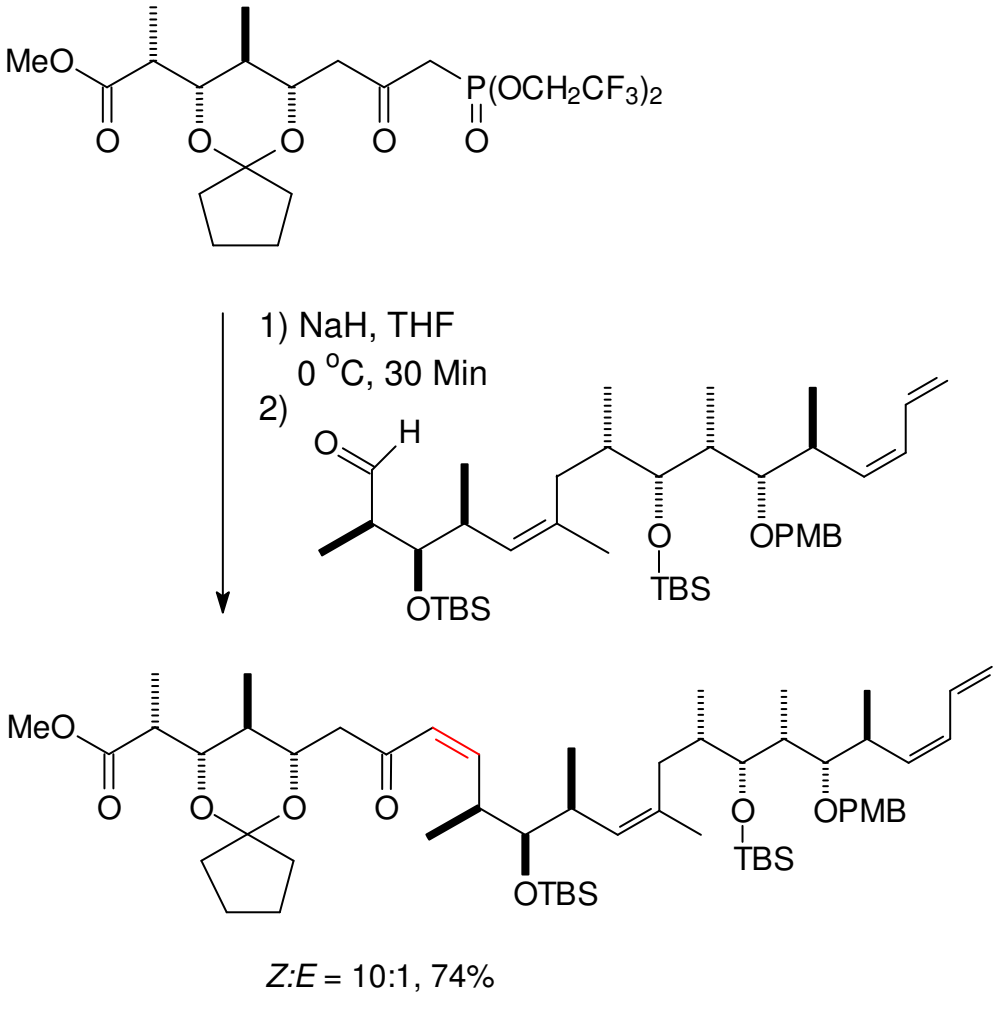
(-)-Dictyostatin



10,11-Dihydrodictyostatin

Figure 2: Structures of antimitotic agents.

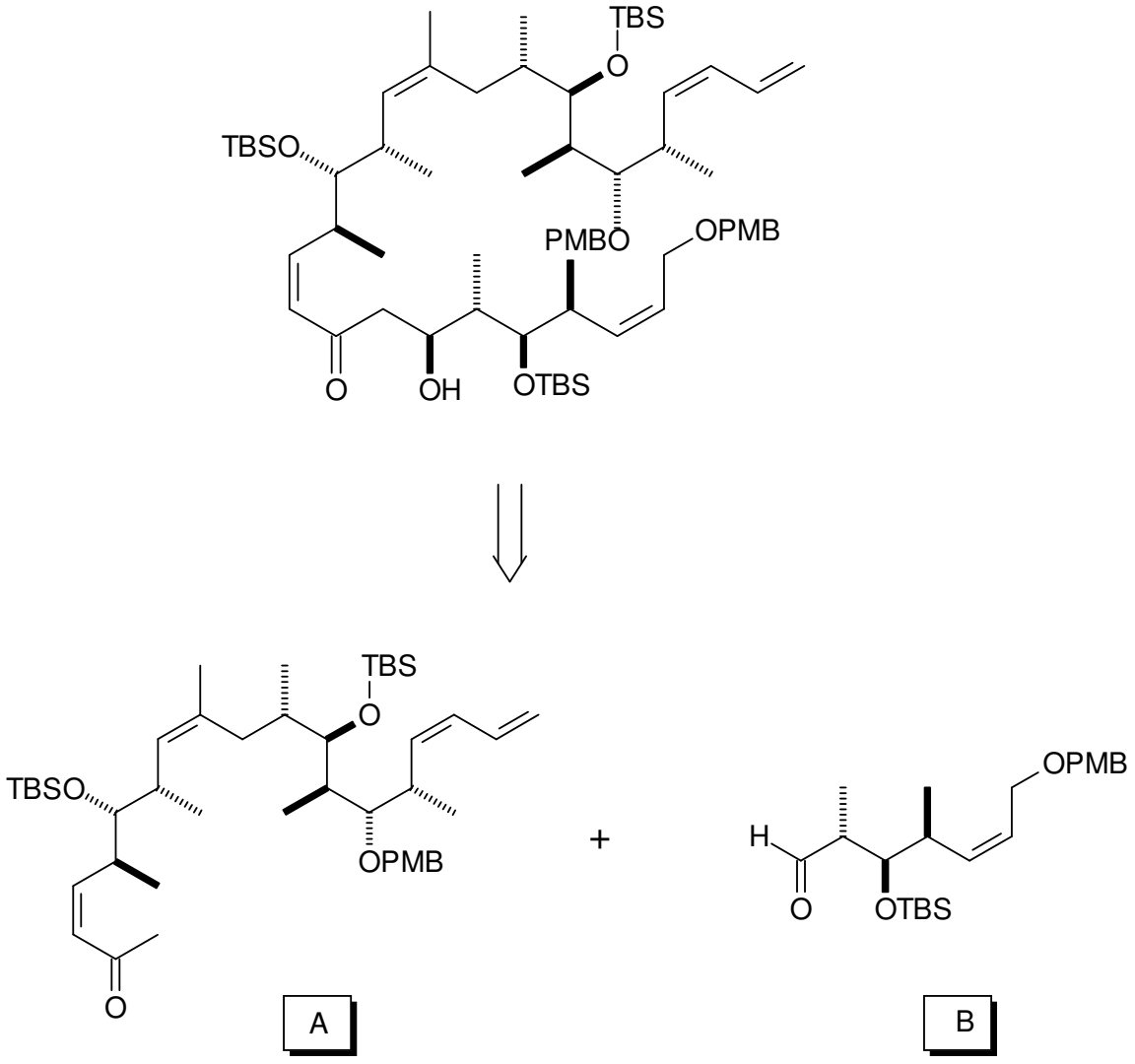
β-Ketophosphonates have been employed in the HWE reaction and variations of the HWE reaction have been used extensively in natural product syntheses.[6-14] Patterson has shown unprecedented usage of advanced bis(2,2,2-trifluoroethyl)-β-ketophosphonates in the Still-Gennari HWE olefination as key steps in the total synthesis of discodermolide, dictyostatin and various analogues of these compounds, thus demonstrating the utility of the Still-Gennari HWE olefination and the practicality of bis(2,2,2-trifluoroethyl)-β-ketophosphonates.[6-13] The key step in a practical synthesis of discodermolide is shown[8] (Scheme 8).



Scheme 8: Key step in Patterson's synthesis of discodermolide.

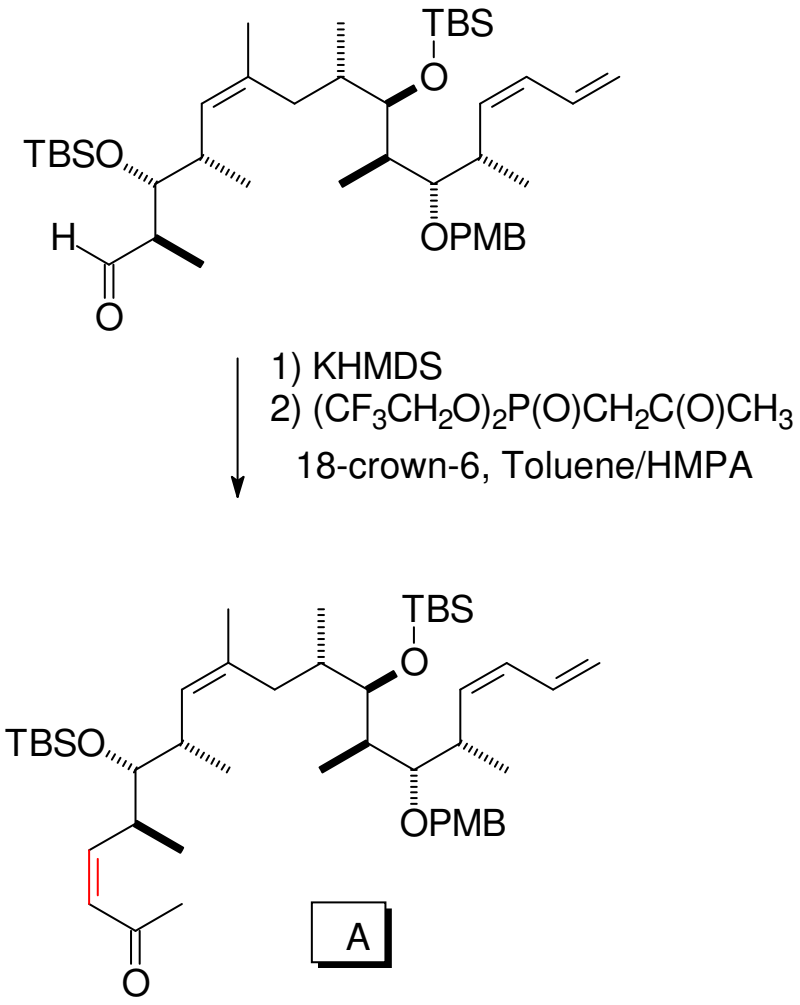
Once the skeleton of the molecule is in hand it becomes a trivial matter of modern synthetic techniques to obtain a sample identical to the natural product.

In the total synthesis of the macrocycle of the hybrid analogue of discodermolide and dictyostatin Patterson employs the Still-Gennari HWE olefination in the key steps of the synthesis of the two fragments (A and B) that make up the skeleton of the hybrid molecule.[11] The retrosynthetic scheme for the skeleton of the precursor to the target hybrid is shown (Scheme 9).

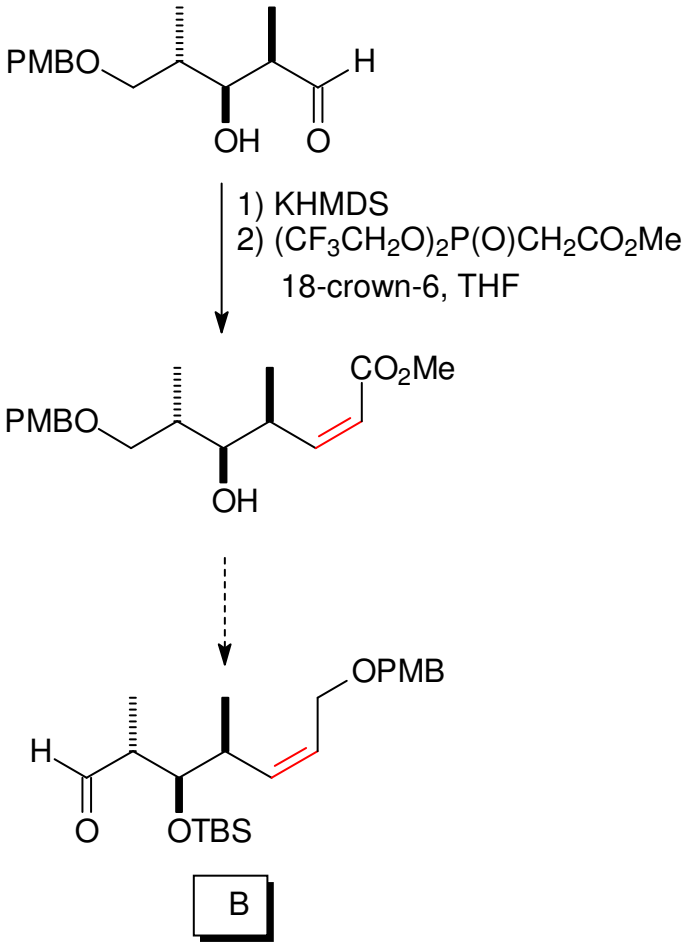


Scheme 9: Retrosynthetic analysis of the hybrid skeleton.

Also shown are the key steps utilizing the Still-Gennari HWE for the formation of fragments A and B (Schemes 10 and 11).



Scheme 10: Application of the Still-Gennari HWE olefination for fragment A.



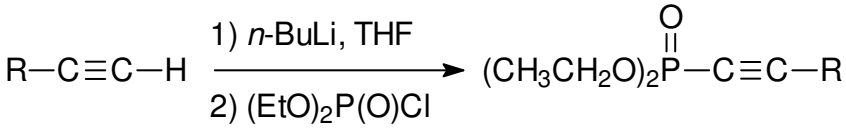
Scheme 11: Application of the Still-Gennari HWE olefination for fragment B.

Following the Still-Gennari olefination in the synthesis of fragment B it becomes a trivial matter of protection and reduction to produce the target compound.

1-Alkynylphosphonates

The first 1-alkynyphosphonate was reported in 1957[19] and their utility as versatile synthetic intermediates in organic syntheses has been realized and investigated. Diethyphosphonoalkynes are most commonly prepared by treating terminal alkynes at -

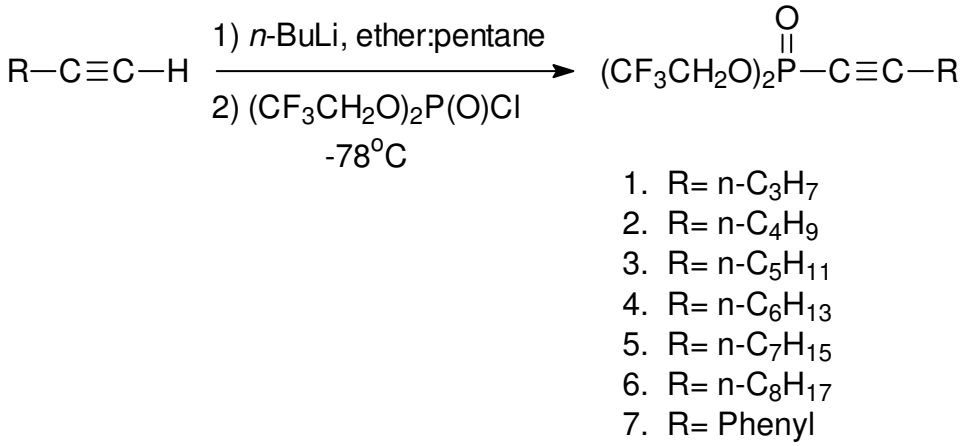
78 ^{o}C with *n*-butyllithium in tetrahydrofuran (THF) to form the lithium-stabilized nucleophilic carbanion which is subsequently allowed to act upon diethyl chlorophosphate. Yields are typically in the range of 80-90% (Scheme 12).[20]



Scheme 12: Synthesis of diethylphosphonoalkynes

The analogous reaction substituting bis(2,2,2-trifluoroethyl) phosphorochloridate for diethyl chlorophosphate initially resulted in a complex mixture that was determined to contain trisalkynylphosphine oxide [$(RCC)_3P=O$] as the major product in addition to significant amounts of unreacted phosphorochloridate, trace amounts of the desired alkynyl phosphonate, as well as the bis alkynyl phosphonate.[28]

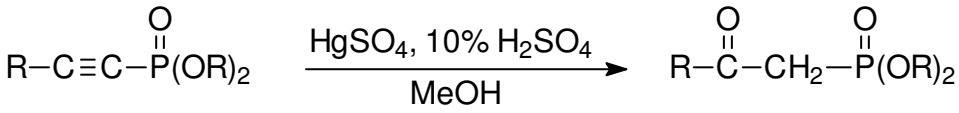
On large scale (50-100 mmol), optimized conditions utilizing a 50:50 ether:pentane solvent system has led to acceptable yields of the bis(2,2,2-trifluoroethyl) phosphonoalkynes. On this scale purification of 10-15 gram quantities in 45-62% yield *via* fractional distillation under high vacuum is possible (Scheme 13).[21, 22]



Scheme 13: Synthesis of bis(2,2,2-trifluoroethyl)phosphonoalkynes.

Reaction of the Triple Bond: Hydration

The triple bond functionality of alkynyl phosphonates is known to undergo many transformations including hydration. The most common method employed in hydrating the triple bond is by way of mercury (II) salts and catalytic aqueous acid. The standard method employs treatment of a stirred solution of the phosphonoalkyne with aqueous 10% H_2SO_4 in the presence of mercury sulfate ($HgSO_4$) in methanol under reflux for 15 hours or at room temperature for 48 hours[23, 24] (Scheme 14).

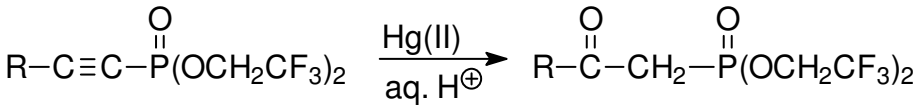


Scheme 14: Standard method of hydration of the alkynyl functional group.

Statement of Purpose

The triple bonds of 1-alkynylphosphonates have been shown to undergo hydration in a Markovnikov fashion in the presence of aqueous acid catalyst and mercury (II) salts using methanol as solvent to yield dialkoxy β-ketophosphonates. However, bis(2,2,2,-trifluoroethyl)-β-ketophosphonates have only been reported to have been formed through the lithium stabilized anion of bis(2,2,2-trifluoroethyl) methylphosphonate acting upon an acid chloride at -98 ^{o}C or alternatively *via* the method reported by Wiemer utilizing treatment of α-halo ketones with two equivalents of strong base to produce the dianion which is subsequently allowed to act upon electrophilic bis(2,2,2-trifluoroethyl) phosphorochloridate at the extremely low temperature of -110 ^{o}C.

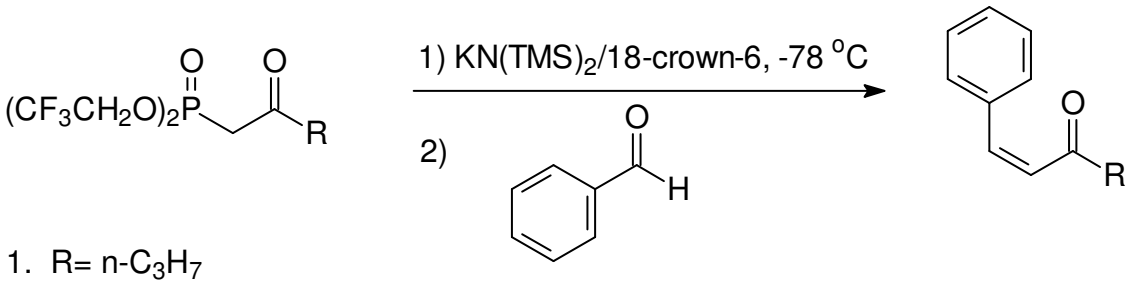
The usefulness of bis(2,2,2,-trifluoroethyl-β-ketophosphonates and the remarkable reactivity of the triple bond of 1-alkynylphosphonates has encouraged us to attempt to develop a complementary acid-catalyzed method for the synthesis of bis(2,2,2,-trifluoroethyl)-β-ketophosphonates from bis(2,2,2-trifluoroethyl) phosphonoalkynes utilizing mercury (II) salts. We hope to develop a method that is not only complementary to that which is already reported, but we also hope to use more easily realized conditions that do not require any special apparatus (Scheme 15).



Scheme 15: Proposed synthesis of bis(2,2,2-trifluoroethyl) phosphonoalkynes.

In addition, should these compounds be prepared under the proposed conditions, we are interested in studying their reactivity in the Still-Gennari HWE olefination and

also in determining the stereochemistry about the double bond in the isolated products (Scheme 16).

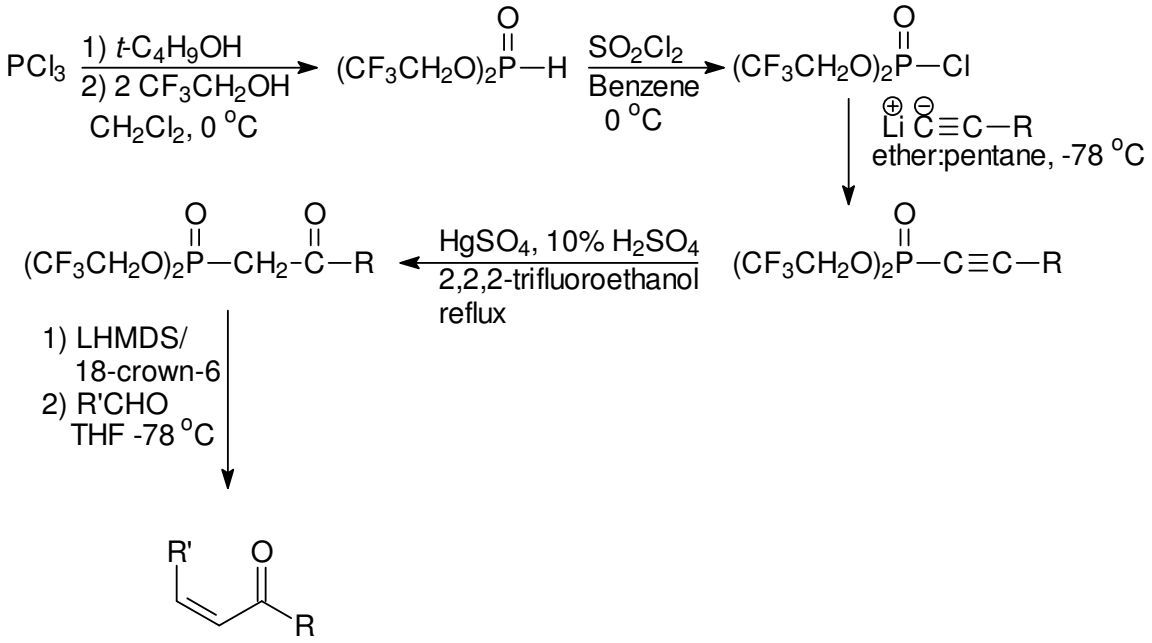


1. R= n-C_3H_7
2. R= n-C_4H_9
3. R= n-C_5H_{11}
4. R= n-C_6H_{13}
5. R= n-C_7H_{15}
6. R= n-C_8H_{17}
7. R= Phenyl

Scheme 16: Proposed Still-Gennari HWE reactions.

Chapter 2: Results and Discussion

This research project was concerned with the development of novel synthetic methods to prepare bis(2,2,2-trifluoroethyl)-β-ketophosphonates which were complementary to those previously reported in the scientific literature and did not require any special apparatus. Additionally we were interested in utilizing readily available materials. Specifically we were interested in the preparation of bis(2,2,2-trifluoroethyl)-β-ketophosphonates from bis(2,2,2-trifluoroethyl) alkynylphosphonates. Assuming the success of our methods we then planned to study the reactivity of these compounds in the Still-Gennari HWE olefination reaction and then to subsequently study the stereochemistry of the products isolated from the HWE reaction. The overall proposed strategies for the synthesis of bis(2,2,2-trifluoroethyl)-β-ketophosphonates and subsequent reactivity studies are illustrated (Scheme 17).

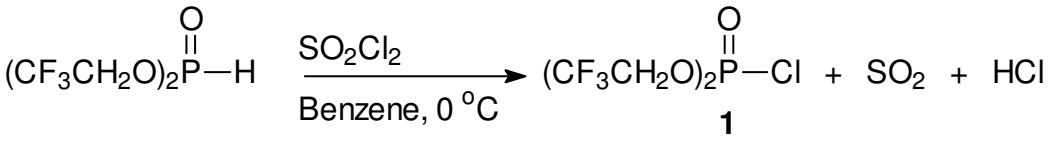


Scheme 17: Overall strategy of the project .

Synthesis of bis(2,2,2-trifluoroethyl) alkynylphosphonates

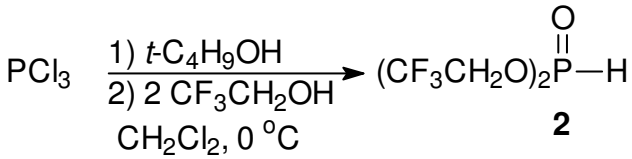
The first step necessarily involved the preparation of bis(2,2,2-trifluoroethyl) alkynylphosphonate compounds as they are not commercially available. The preparation of bis(2,2,2-trifluoroethyl) alkynylphosphonates involved methods developed and optimized by former members of the Jackson lab from commercially available terminal alkynes and bis(2,2,2-trifluoroethyl) phosphorochloridate.[28] This synthesis involves treating the terminal alkynes with *n*-butyllithium at -78 ^{o}C utilizing a 50:50 ether:pentane solvent system to form the lithium-stabilized carbanion nucleophile *in situ* which was subsequently allowed to act upon the bis(2,2,2-trifluoroethyl) phosphorochloridate.[28] All syntheses proceeded smoothly and in moderate to good yield with the exception of the reaction utilizing phenyacetylene as our terminal alkyne (compound **9**, Table 1). Since the desired product was not isolated from this reaction in our initial attempts it was decided to attempt the reaction using one equivalent of hexamethylphosphoramide (HMPA). Many reactions proceed more readily in the presence of HMPA because of its strong dipole. HMPA is known to promote coordination of the metal counter ion, thus making the carbanion more nucleophilic. This methodology proved to be successful in the respect that pure product was isolated, although in low yield (1.63 g, 10%). However, this was enough material for further studies and because HMPA is extremely toxic and a known carcinogen further attempts to optimize this reaction utilizing this methodology were discontinued. However, other less toxic solvents that also have a strong dipole and are known to promote metal counterion coordination such as *N,N*'-dimethylpropyleneurea (DMPU) could be substituted and would be a worthwhile endeavor for future attempts at improving yields utilizing this methodology.

The bis(2,2,2-trifluoroethyl) phosphorochloridate used in the preparation of our phosphonoalkynes was also synthesized. This was accomplished by the action of sulfuryl chloride in benzene upon a solution of bis(2,2,2-trifluoroethyl) phosphite also in benzene.[29, 30] The conditions for this method of preparation are well optimized and therefore proceeded smoothly and in good yield (>75%). This synthesis is depicted (Scheme 18).



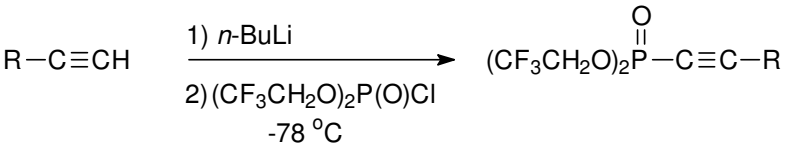
Scheme 18: Synthesis of bis(2,2,2-trifluoroethyl) phosphorochloridate.

Because we were interested in preparing our bis(2,2,2-trifluoroethyl) alkynylphosphonates on large scale (100 mmol) for use in further studies, we sought to find a method for the preparation of the bis(2,2,2-trifluoroethyl) phosphite. A general method for the preparation of bis(2,2,2-trifluoroethyl) phosphite utilizing one equivalent of phosphorus trichloride and one equivalent of 2-methyl-2-propanol followed by the addition of two equivalents of 2,2,2-trifluorethanol (TFE) at 0 ^{o}C utilizing dichloromethane as the solvent was settled upon and provided satisfactory results.[31] Employing this procedure we were able to reliably obtain approximately 100 gram quantities of bis(2,2,2-trifluoroethyl) phosphite that were substantially more pure than what was previously available to us commercially and at a fraction of the cost. This method is depicted (Scheme 19).



Scheme 19: Gibbs synthesis of bis(2,2,2-trifluoroethyl) phosphate.[31]

A summary of the bis(2,2,2-trifluoroethyl) alkynylphosphonates that were prepared are summarized (Table 1).



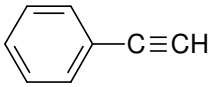
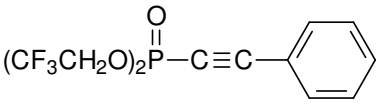
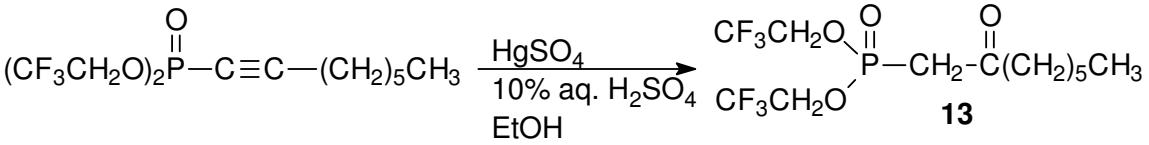
Entry	Alkyne	Alkynylphosphonate	Compound	Isolated Yield
(1a)	$CH_3(CH_2)_2C\equiv CH$	$(CF_3CH_2O)_2P(O)-C\equiv C(CH_2)_2CH_3$	**3**	52%
(1b)	$CH_3(CH_2)_3C\equiv CH$	$(CF_3CH_2O)_2P(O)-C\equiv C(CH_2)_3CH_3$	**4**	62%
(1c)	$CH_3(CH_2)_4C\equiv CH$	$(CF_3CH_2O)_2P(O)-C\equiv C(CH_2)_4CH_3$	**5**	39%
(1d)	$CH_3(CH_2)_5C\equiv CH$	$(CF_3CH_2O)_2P(O)-C\equiv C(CH_2)_5CH_3$	**6**	50%
(1e)	$CH_3(CH_2)_6C\equiv CH$	$(CF_3CH_2O)_2P(O)-C\equiv C(CH_2)_6CH_3$	**7**	59%
(1f)	$CH_3(CH_2)_7C\equiv CH$	$(CF_3CH_2O)_2P(O)-C\equiv C(CH_2)_7CH_3$	**8**	46%
(1g)			**9**	10%

Table 1: Yields of bis(2,2,2-trifluoroethyl) alkynylphosphonates

Synthesis of bis(2,2,2-trifluoroethyl) β-ketophosphonates

Once the required alkynylphosphonates were in hand the hydration of the triple bond was attempted utilizing mercury sulfate ($HgSO_4$) and 10% aqueous sulfuric acid with absolute ethanol as solvent. In the initial attempt two reactions were set up and ran simultaneously using bis(2,2,2-trifluoroethyl) octynylphosphonate to make the corresponding β-ketophosphonate, bis(2,2,2-trifluoroethoxy)phosphono-octanone (Scheme 20). In order to observe the effects of temperature on these reactions one reaction was allowed to stir at room temperature while the other was gently refluxed; both reactions were monitored using ^{31}P NMR. The initial results were encouraging as the starting material peak had begun to diminish in both reactions. Although multiple peaks were observed in the ^{31}P NMR spectra throughout the monitoring of both reactions, it was observed that as the reaction progressed over time one of the newly formed peaks which was believed to be the peak of the desired compound in the ^{31}P NMR spectra stayed the same or slightly decreased in intensity as another peak increased in intensity. What we believed we were observing was the hydrolysis of the phosphonate ester(s). The desired target molecule is compound **6,** Scheme 20 and it was initially isolated in 44 % yield. All other possible products are a result of the hydrolysis of the phosphonate ester(s) by water that is necessarily present under the stated conditions and are depicted in Figure 3.



Scheme 20: Hydration of bis(2,2,2-trifluoroethyl) octynylphosphonate.

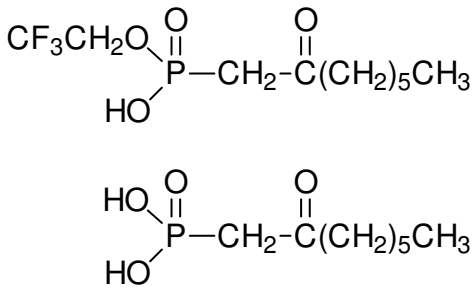


Figure 3: Possible hydrolysis products from Scheme 20.

Furthermore it was observed that temperature played a dramatic affect on this reaction. In the reaction run at room temperature less than one half of the starting material had been consumed after 72 hours according to ^{31}P NMR. Even though the initial major peak was believed to be our product of interest, a second peak had begun to amplify in intensity with little gain or even diminished intensity of the desired peak. The crude reaction mixture conducted under reflux conditions also displayed multiple peaks in the ^{31}P NMR spectrum. The major peak however was believed to be the desired product and the hydrolysis peaks were much lower in intensity than the reaction run at room temperature. This hypothesis was confirmed by ^{1}H NMR after subsequent purification of the reaction run under refluxing conditions. The ^{1}H NMR spectrum exhibited the characteristic 4H signal of an overlapping doublet of quartets corresponding to the two sets of equivalent methylene protons of the phosphonate esters in the expected region of approximately 4.5 ppm (figure 4):

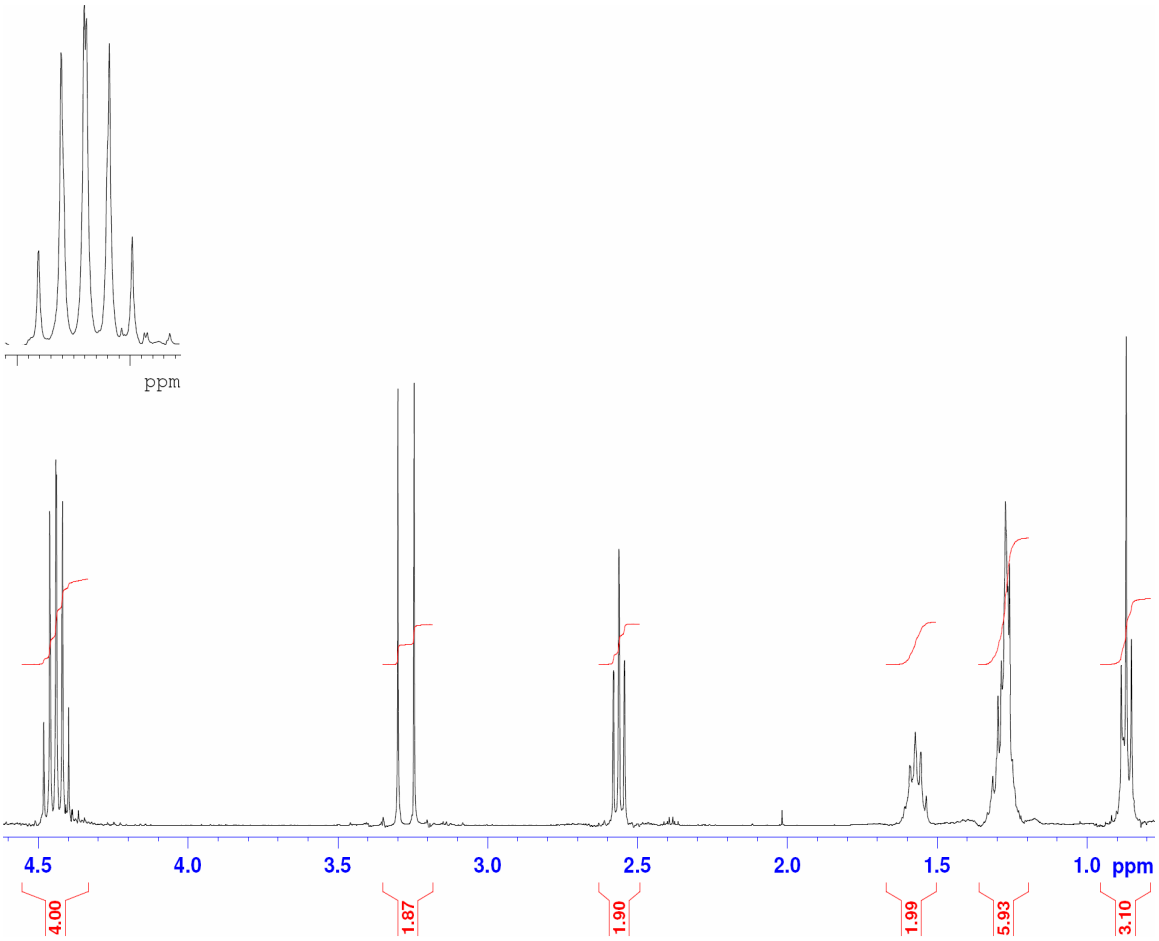


Figure 4: ^{1}H NMR spectrum of bis(2,2,2-trifluoroethoxy)-phosphono-octanone

This doublet of quartet splitting pattern arises from the fact that the methylene protons are coupled to the three fluorine atoms (I =1/2) on the adjacent carbon atom. Therefore, the signal is split into a quartet. Since these methylene protons are also coupled to phosphorus (I=1/2) the quartet signal is split into a doublet resulting in the observed doublet of quartets. Since $J_1 \approx J_2$ we observe overlapping of the quartets.

Based on these results it was decided that all subsequent hydration reactions should be conducted under gentle reflux conditions. It was believed that the hydrolysis could be controlled and the formation of the desired product favored utilizing a gentle reflux and careful monitoring of the progress of the reaction by ^{31}P NMR. Additionally

2,2,2-trifluoroethanol was substituted for the absolute ethanol as the solvent. Indeed we were pleased to learn that this substitution under very light reflux and careful monitoring of the reaction's progress predominantly yielded the desired compound according to ^{31}P, ^{1}H, and ^{13}C NMR data. The desired compound was easily isolated and purified using flash column chromatography. Because the hydrolysis products are much more polar and therefore elute much later, a clean separation was easily accomplished. The best yield on a 1 mmol scale was 81% in the hydration of bis(2,2,2-trifluoroethyl) pentynyl phosphonate.

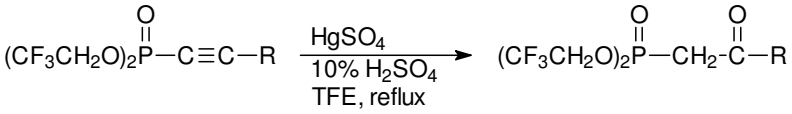
Having the good fortune of isolating the desired compound in pure form we wished to scale up the process (50-100 mmol) for further studies, and we next wished to study the reactivity of our newly synthesized compounds in the Still-Gennari HWE reaction. These scaled up syntheses of bis(2,2,2-trifluoroethyl)-β-ketophosphonates gave adequate yields of pure product according to ^{31}P, ^{1}H , and ^{13}C NMR for further studies.

Later it was thought that if the aprotic solvent THF was substituted for 2,2,2-trifluorethanol that the hydrolysis products might be avoided all together and that yields could be improved. However, the hydrolysis products were almost entirely observed in the ^{31}P NMR spectrum and the desired product was not isolated.

The most serious problem that arose in the scaled up synthesis of bis(2,2,2-trifluoroethyl)-β-ketophosphonates utilizing this methodology was realized during the purification scheme. An elusive white compound which was believed to be some form of mercury salt was first observed while running the flash chromatography column. This compound was observed to form a thin layer on the bed of sand atop of the silica thus effectively plugging the column. Furthermore, this material was observed to be present as

a contaminant after the desired product was isolated. Removal of this compound was tedious and resulted in diminished yields. An aqueous wash did nothing to prevent contamination as this compound appeared to be insoluble in water. This compound was believed to be semi-soluble in chloroform and so ether was substituted in the initial extraction procedure after work up, but this led to an unacceptable emulsion. Several other methods were employed to remove this compound, the first of which was an attempted filtration through celite, but this method proved ineffective as much of this compound passed through the celite resulting in contamination of the final product. Several filtrations through number 42 porosity filter paper initially seemed to be most effective and often removed evidence of the contaminant. However, this method was time consuming, resulted in greatly diminished yields, and was not 100% effective.

The most effective method discovered for the removal of this contaminant seemed to be an aqueous wash with a 1 M potassium iodide solution prior to the extraction into chloroform whereby the contaminant was converted to a bright orange water-soluble salt. The crude product was then extracted into chloroform with no evidence of the contaminant following subsequent purification *via* flash column chromatography. On a larger scale purification through fractional distillation under high vacuum may be possible. However, this method was not tried since significant amounts of substantially pure quantities of the desired compounds were obtained under the methods previously discussed. A depiction of the prepared bis(2,2,2-trifluoroethyl)-β-ketophosphonates is summarized (Table 2).



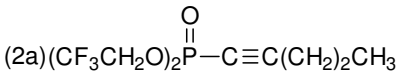
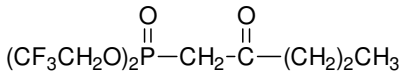
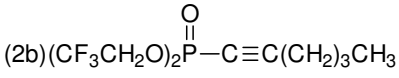
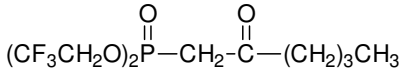
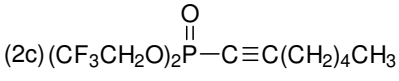
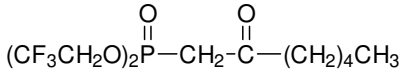
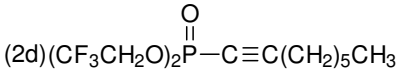
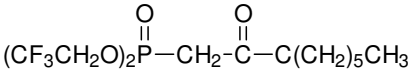
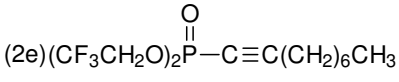
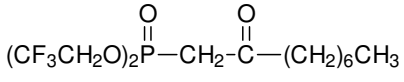
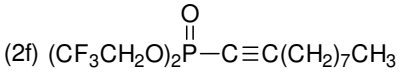
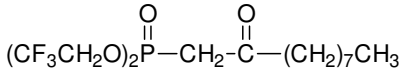
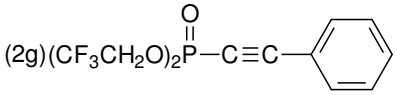
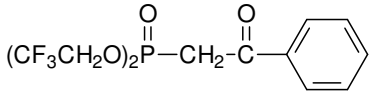
Entry	Alkynylphosphonate	β-Ketophosphonate	Compound	Isolated Yield
(2a)			**10**	66%
(2b)			**11**	81%
(2c)			**12**	57%
(2d)			**13**	52%
(2e)			**14**	45%
(2f)			**15**	46%
(2g)			**16**	23%

Table 2: Yields of prepared bis(2,2,2-trifluoroethyl)-β-ketophosphonates

Still-Gennari HWE Utilizing Bis(2,2,2-trifluoroethyl) β-Ketophosphonates

Now that a significant number of bis(2,2,2-trifluoroethyl)-β-ketophosphonates were prepared, isolated, and purified we next were interested in studying their reactivity in the Still-Gennari HWE olefination reaction. We were also interested in assigning the stereochemistry about the newly formed double bond in the isolated products. Benzaldehyde was readily available and therefore it was the aldehyde chosen to conduct this study.

We duplicated the conditions reported by W. C. Still and C. Gennari of their originally published paper in 1983[16] using one equivalent of potassium hexamethyldisilazide as the base, five equivalents of 18-crown-6, and utilizing anhydrous THF as the solvent. The β-ketophosphonate was combined with 18-crown-6 in THF and subsequently cooled to -78 ^{o}C. In accord with Wiemer's study on temperature effects on stereocontrol in the Horner-Wadsworth-Emmons condensation of phosphono lactones[32] it was verified that it was imperative to keep the reaction at -78 ^{o}C in order to obtain exclusive formation of the (*Z*) adduct. It was observed that if the addition of the KHMDS or the aldehyde was too rapid the isolated product contained a mixture of *Z : E* isomers and therefore it was mandatory that the addition of KHMDS was performed in a slow dropwise manner such that -78 ^{o}C was maintained. To ensure slow addition of the aldehyde a 1 in 10 dilution of benzaldehyde in THF was prepared thus reducing the amount of reactant introduced over time and thereby aiding in the maintenance of the required -78 ^{o}C reaction temperature. It should also be noted that the reaction was not allowed to warm prior to quenching with saturated ammonium chloride. Under the prescribed conditions the results of the HWE reaction gave exclusively the *Z*-isomer in good to excellent yield.

The stereochemistry about the double bond in the final product was characterized through ^{1}H NMR studies. Since the vicinal protons about a double bond differ in their coupling constants (^{3}J) depending on whether they are *cis* or *trans* (*Z*-isomer or *E*-isomer respectively), with the *cis* isomer having the smaller coupling constant ($J \approx 12.7$ Hz) and the trans isomer possessing the larger coupling constant ($J \approx 16.2$ Hz), a simple ^{1}H NMR experiment may easily be employed to elucidate which isomer is present in a sample or

alternatively the ratio of *E*:*Z* if a mixture is present. These concepts are illustrated (Figure 5 and Figure 6).

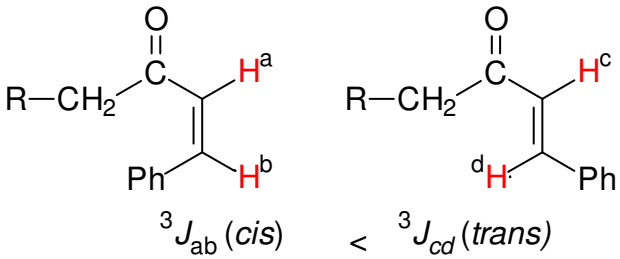


Figure 5: Illustration of coupling between *cis* versus *trans* protons.

A typical spectrum of the *Z*-isomer produced from an HWE reaction utilizing a bis(2,2,2-trifluoroethyl) β-ketophosphonate is illustrated (Figure 6).

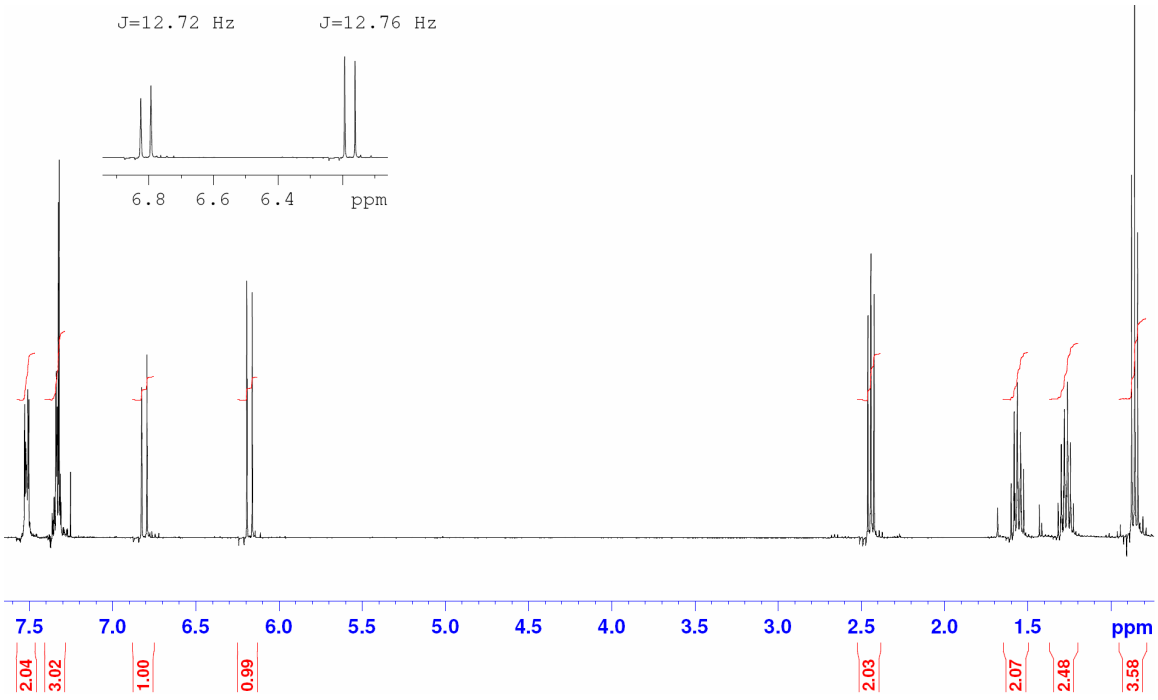


Figure 6: ^{1}H spectrum of an HWE product: (*Z)* 1-phenyl-1-hepten-3-one, compound **17.**

A summary of the results of the HWE products are illustrated (Table 3).

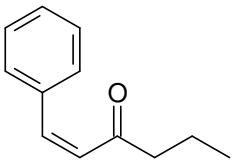
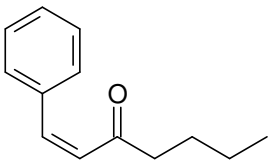
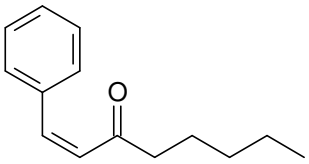
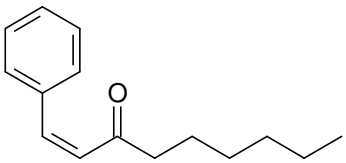
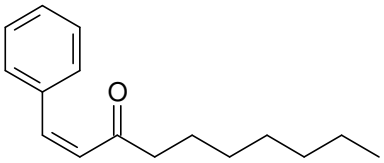
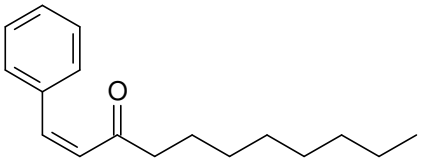
Entry	Beta-Ketophosphonate	HWE Product	Compound	*Z:E* / (Yield)
(3a)	$(CF_3CH_2O)_2P(O)-CH_2-C(=O)-(CH_2)_3CH_3$		**17**	100:0 (86%)
(3b)	$(CF_3CH_2O)_2P(O)-CH_2-C(=O)-(CH_2)_2CH_3$		**18**	100:0 (53%)
(3c)	$(CF_3CH_2O)_2P(O)-CH_2-C(=O)-(CH_2)_4CH_3$		**19**	100:0 (89%)
(3d)	$(CF_3CH_2O)_2P(O)-CH_2-C(=O)-C(CH_2)_5CH_3$		**20**	100:0 (79%)
(3e)	$(CF_3CH_2O)_2P(O)-CH_2-C(=O)-(CH_2)_6CH_3$		**21**	100:0 (69%)
(3f)	$(CF_3CH_2O)_2P(O)-CH_2-C(=O)-(CH_2)_7CH_3$		**22**	100:0 (94%)

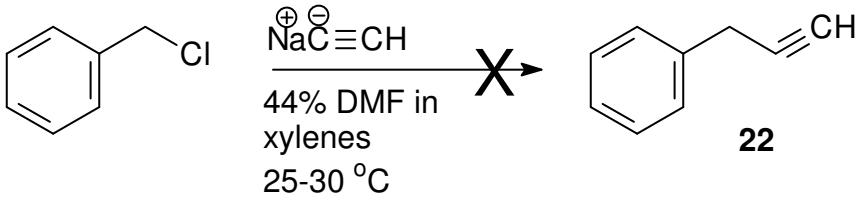
Table 3: Results of HWE reaction utilizing prepared β-ketophosphonates.

Attempted Preparation of Alkynes

Our good fortune in the preparation of the previously described β-ketophosphonates from terminal alkynes encouraged us to attempt the synthesis of more sophisticated alkynylphosphonates from more complex terminal alkynes. Our first step in this endeavor was to attempt syntheses of more complex terminal alkynes from sodium acetylide and alkyl halides.

3-phenyl-1-propyne

Because the synthesis of 2-phenyl-1-ethynylphosphonate utilizing phenylacetylene (compound **9**) was problematic the first attempted alkyne synthesis was 3-phenyl-1-propyne (**22**) from benzyl chloride and sodium acetylide (Scheme 21).



Scheme 21: Proposed reaction towards the synthesis of 3-phenyl-1-propyne.

The solvent system in Scheme 21 was based on work done by T. F. Rutledge on the synthesis of alkyl acetylenes from sodium acetylide.[33] Disappointingly as depicted in Scheme 21 the reaction failed to give the desired product. However, it was noticed that crystals had formed at the bottom of the flask and upon analysis by X-ray crystallography they were identified as a pure compound for which the crystal structure had not been previously published. We believe this compound was first described in 1937 by T. H. Vaughn et al, [34] but its structure has not been elucidated until now. We have identified

this compound formed from benzyl chloride and sodium acetylide as 2,5-dibenzyl-1,2,5,6-tetraphenyl-3-hexyne and is shown (Figure 7).

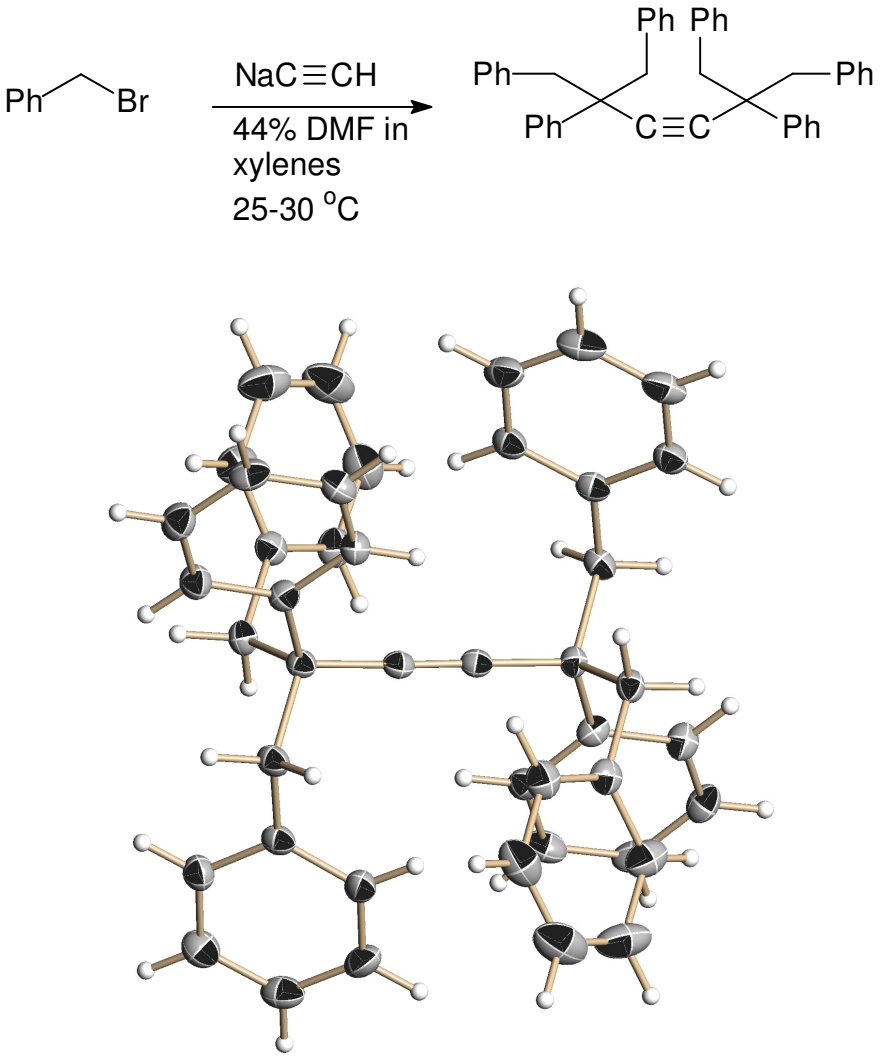


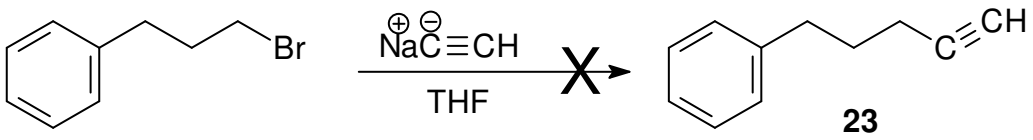
Figure 7: X-ray crystal structure of 2,5-dibenzyl-1,2,5,6-tetraphenyl-3-hexyne.

The elucidation of the mechanism for the formation of 2,5-dibenzyl-1,2,5,6-tetraphenyl-3-hexyne is currently underway by members of the Jackson lab. Once the reaction is shown to be reproducible it will be run and aliquots of the reaction will be quenched at various points in time utilizing deuterated water. By analysis of the deuterated products after quenching a mechanism will be proposed.

Another attempt was made towards the synthesis of 3-phenyl-1-propyne using a 10% excess of sodium acetylide and changing the solvent to THF. Disappointingly the desired product was not formed, and at this point we decided to move on and attempt syntheses of other terminal alkynes.

5-phenyl-1-pentyne

We next attempted to synthesize 5-phenyl-1-pentyne utilizing 1-bromo-3-phenyl-propane and sodium acetylide. The reaction conditions are depicted (Scheme 23):



Scheme 23: Attempted synthesis of 5-phenyl-1-pentyne

Unfortunately this synthesis also failed to yield the desired compound, and the reaction only returned starting materials according to NMR analysis. Regrettably further attempts at the synthesis of terminal alkynes were suspended.

Summary and Conclusions

In summary we have shown that we indeed were able to form bis(2,2,2,-trifluoroethoxy)-β-ketophosphonates through the hydration of bis(2,2,2,-trifluoroethoxy)-alkynylphosphonates utilizing $HgSO_4$ and 10% aqueous sulfuric acid. Our methods are complementary to those previously reported and have been shown to be reproducible to give respectable to good yields. In total we have prepared seven unreported compounds by this method. We have also shown that these compounds are useful in preparing the (*Z*)-α,β-unsaturated ketones *via* the Still-Gennari Horner-Wadsworth-Emmons olefination. Furthermore in our quest to synthesize alkynes for the preparation of more complicated phosphonoalkynes we have elucidated the crystal structure of a previously reported compound. Although this compound was previously reported its identity was unknown. This discovery has prompted a mechanistic study and elucidation of the mechanism by which the compound was formed is currently underway by other members of the Jackson group. Despite the success and results of this research project further studies would be worthwhile. These endeavors could include attempts to develop methods toward the synthesis of more variegated phosphonoalkynes from more complex terminal alkynes. The synthesis of the corresponding β-ketophosphonates could then be attempted through hydration. It might also be interesting and worthwhile to attempt to utilize other mercury salts such as $HgCl_2$ in lieu of $HgSO_4$ in future β-ketophosphonates hydrations reactions.

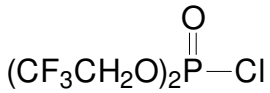
Chapter 3: Experimental

General Methods

Pentane was distilled from CaH_2 prior to use, and THF was distilled from sodium-benzophenone ketyl. All other commercial reagents were purchased from Aldrich or Acros and used without further purification unless otherwise stated. All solvents were dried or distilled by standard techniques. Flash chromatography was conducted with Merck grade 9385, 230-400 mesh, 60 Å silica. Thin layer chromatography (TLC) was conducted on aluminum backed silica plates. Visualization was accomplished utilizing an ultraviolet lamp and staining with a 5% phosphomolybdic acid (PMA) in ethanol, followed by heating. An iodine chamber was utilized in staining the bis(2,2,2-trifluoroethyl) β-ketophosphonates and a $KMnO_4$ solution was employed in visualizing the α,β-unsaturated ketone products of the Still-Gennari HWE olefination reaction.

NMR spectra (^{31}P, ^{13}C, and ^{1}H) were recorded with a Varian Gemini 2000, 400 MHz spectrometer, or a Bruker Avance AG 400 MHz spectrometer using deuterochloroform as the solvent. The ^{1}H chemical shifts are reported in parts per million (ppm) downfield from internal $(CH_3)_4Si$ (0 ppm). The ^{13}C chemical shifts are reported in parts per million (ppm) downfield from $(CH_3)_4Si$ with $CDCl_3$ as the internal standard (77.0 ppm). ^{31}P chemical shifts are reported in parts per million downfield from H_3PO_4 (external standard). Coupling constants are reported in hertz (Hz). The crystal structure was elucidated using X-ray crystallography on a Bruker-Nonius Smart Apex CCD Diffractometer.

Bis(2,2,2-trifluoroethyl) phosphorochloridate (1).

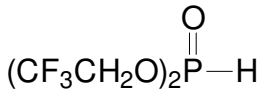


All glassware was previously dried overnight. Bis(2,2,2 trifluoroethyl) phosphite (25 g, ~ 0.1 mol) was quantitatively transferred to a 250 mL round bottom flask containing benzene (30 mL). The reaction vessel was cooled to 0 ºC, fitted with a reflux condenser. The top of the condenser was fit with an addition funnel. The addition funnel was charged with benzene (30 mL), sulfuryl chloride (10.15 mL, 0.1 mol), and put under the positive pressure of argon. The contents of the addition funnel were added dropwise to the bis(2,2,2 trifluoroethyl) phosphite solution and the reaction allowed to stir overnight. The benzene was removed by rotary evaporation and the product fractionally distilled to yield bis(2,2,2 trifluoroethyl) phosphorochloridate (25.65 g, 73%) as a clear oily liquid.

^{31}P NMR ($CDCl_3$) δ 5.67.

^{1}H NMR ($CDCl_3$) δ 4.43-4.58 (m, 4 H).

Bis(2,2,2-trifluoroethyl) phosphite (2).[31]

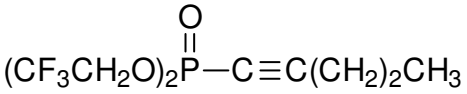


All glassware was previously dried overnight. A solution of 2-methyl-2-propanol (37.0 g, 0.5 mol) in dichloromethane (100 mL) was added dropwise to a stirred solution of phosphorus trichloride (43.5 mL, 0.5 mol) in dichloromethane (100 mL) under an atmosphere of argon over a period of 45 minutes. After the addition was complete the reaction mixture was stirred for an additional 30 minutes at 0-5 ºC; after which time a solution of 2,2,2-trifluoroethanol (100 g, 1 mol) in dichloromethane (100 mL) was added dropwise over the course of 30 minutes. The temperature was maintained in the range of

0-5 ºC. Stirring was continued under a stream of argon for a period of 16 hours to remove excess HCl byproduct. The dichloromethane was removed by rotary evaporation and the final product fractionally distilled under high vacuum to produce bis(2,2,2 trifluoroethyl) phosphite (98.37 g, 80%) as a clear oily liquid.

Bis(2,2,2 trifluoroethyl) phosphonoalkynes:

Bis(2,2,2-trifluoroethyl) pent-1-ynylphosphonate (3).



Due to the volatile nature of 1-pentyne the ampule was cooled to -78 ºC prior to opening, and then transferred to an argon flushed 500 mL round bottom flask (4.93 mL, 50 mmol) containing a magnetic stir bar and 300 mL of pentane and diethyl ether (50:50). The reaction vessel was cooled to -78 ºC and put under the positive pressure of argon using a rubber septum and argon filled balloon fit to the top of the flask. Stirring was commenced, and the addition of *n*-butyllithium (34.4 mL, 50 mmol, 1.6 M in hexanes) dropwise *via* syringe over a period of 30 minutes was begun. After the addition of *n*-butyllithium was complete the reaction was stirred for an additional 1 hour; after which time the reaction mixture was allowed to warm at room temperature for approximately 1 hour to aid in the formation of the carbanion nucleophile. After this warming period the reaction mixture was cooled back down to -78 ºC and stirred for an additional 2 hours. Finally bis(2,2,2-trifluoroethyl) phosphorochloridate (9.3 mL, 56 mmol) was added dropwise *via* syringe over a period of approximately 20 minutes and the reaction mixture allowed to stir overnight. The reaction was quenched using saturated ammonium chloride (3x50 mL) and subsequently washed with water (3x50 mL) to remove excess salts. The product was extracted into ether (3x50 mL), dried over anhydrous magnesium sulfate,

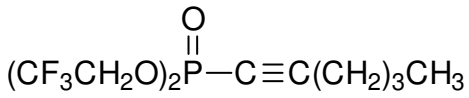
and filtered. The solvent was removed by rotary evaporation and fractionally distilled under high vacuum to yield compound **3** (32.7 g, 52%) as a clear and colorless viscous oil.

^{31}P NMR ($CDCl_3$) δ -5.63.

^{1}H NMR ($CDCl_3$) δ 1.05 (t, *J* = 7.4 Hz, 3H), 1.65 (sextet, *J* = 7.3 Hz 2H), 2.41 (dt, *J* = 7.0, 4.8 Hz, 2H), 4.43 (dq , *J* = 8.4, 8.0 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 12.79 (s), 20.41 (d, *J* = 2.2 Hz), 20.77 (d, *J* = 4.4 Hz), 62.41 (2, dq, *J* = 38.4, 4.4 Hz), 67.29 (d, *J* = 330.9 Hz), 106.65 (d, *J* = 58.7 Hz), 122.17 (2, dq, *J* = 277.4, 9.9 Hz).

Bis(2,2,2-trifluoroethyl) hex-1-ynylphosphonate (4).



1-Hexyne (5.75 mL, 50 mmol) was transferred to an argon flushed 500 mL round bottom flask containing 300 mL 50:50 pentane and diethyl ether, and a magnetic stir bar. The reaction vessel was cooled to -78 ºC and put under the positive pressure of argon using a rubber septum and argon filled balloon fit to the top of the flask. The reaction was stirred and the addition of *n*-butyllithium (34.4 mL, 50 mmol, 1.6 M in hexanes) dropwise *via* syringe over a period of 30 minutes was begun. After the addition of *n*-butyllithium was complete the reaction was stirred for an additional 1 hour; after which time the reaction mixture was allowed to warm at room temperature for approximately 1 hour. After warming the reaction mixture was cooled back down to -78 ºC and stirred for an additional 2 hours. Finally bis(2,2,2-trifluoroethyl) phosphorochloridate (9.3 mL, 56 mmol) was added dropwise *via* syringe over a period of approximately 20 minutes and the reaction mixture allowed to stir overnight. The reaction was quenched using saturated

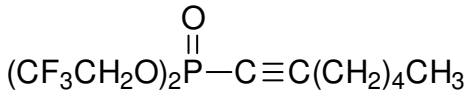
ammonium chloride (3x50 mL) and subsequently washed with water (3x50 mL) to remove any excess salts. The reaction mixture was extracted with ether (3x50 mL) then dried over anhydrous magnesium sulfate and subsequently filtered. The solvent was removed by rotary evaporation and fractionally distilled under high vacuum to yield compound **4** (10.1 g, 62%) as a clear and colorless viscous oil.

^{31}P NMR ($CDCl_3$) δ -5.05.

^{1}H NMR ($CDCl_3$) δ 0.90 (t, *J* = 7.3 Hz, 3H), 1.40 (sextet, *J* = 7.4 Hz, 2H), 1.56 (quintet, *J* = 7.3 Hz, 2H), 2.37 (dt, *J* = 7.1, 4.7 Hz, 2H), 4.36 (dq, *J* = 8.29, 8.01 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.27 (s), 18.92 (d, *J* = 4.8 Hz), 21.82 (s), 29.02 d, *J* = 2.2 Hz), 62.57 (2, dq, *J* = 38.2, 4.2 Hz), 67.31 (d, *J* = 331.0 Hz), 107.18 (d, *J* = 58.8 Hz), 122.12 (2, dq, *J* = 277.0, 10.2 Hz).

Bis(2,2,2-trifluoroethyl) hept-1-ynylphosphonate (5).



1-Heptyne (6.56 mL, 50 mmol) was transferred to an argon-flushed 500 mL round bottom flask containing a magnetic stir bar and 300 mL of pentane and diethyl ether (50:50). The reaction vessel was cooled to -78 ºC and put under the positive pressure of argon using a rubber septum and argon-filled balloon fitted to the top of the flask. Stirring was commenced. The addition of *n*-butyllithium (34.4 mL, 50 mmol, 1.6 M in hexanes) in a dropwise manner *via* syringe over a period of 30 minutes was begun. After the addition of *n*-butyllithium was completed the reaction was stirred for an additional 1 hour and the reaction mixture was allowed to warm at room temperature for approximately 1 hour. After the warming period the reaction mixture was cooled back down to -78 ºC and stirred for an additional 2 hours. Finally bis(2,2,2- trifluoroethyl) phosphorochloridate

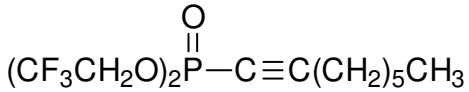
(9.3 mL, 56 mmol) was added dropwise through syringe over a period of approximately 20 minutes and the reaction mixture allowed to stir overnight. The reaction was quenched using saturated ammonium chloride (3x50 mL) and subsequently washed with water (3x50 mL) to remove excess salts. The product was extracted into ether (3x50 mL), dried over anhydrous magnesium sulfate and filtered. The solvent was removed by rotary evaporation and fractionally distilled under high vacuum to yield compound **5** (6.6 g, 39%) as a clear and colorless viscous oil.

^{31}P NMR ($CDCl_3$) δ -5.01.

^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.40-1.25 (m, 4H), 1.58 (quintet, *J* = 7.3 Hz, 2H), 2.36 (dt, *J* = 7.2, 4.7 Hz, 2H), 4.36 (dq, *J* = 8.3, 7.9 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.56 (s), 19.08 (d, *J* = 5.1 Hz), 21.86 (s), 26.65 (d, *J* = 2.9 Hz), 30.73 (s), 62.56 (2, dq, *J* = 38.3, 4.4 Hz), 67.32 (d, *J* = 331.5 Hz), 107.34 (d, *J* = 58.55 Hz), (2, dq, *J* = 277.6, 10.2 Hz).

Bis(2,2,2 trifluoroethyl) oct-1-ynylphosphonate (6).



1-Octyne (7.37 mL, 50 mmol) was transferred to an argon-flushed 500 mL round bottom flask containing a magnetic stir bar and 300 mL of pentane and diethyl ether (50:50). The reaction vessel was cooled to -78 ºC and put under the positive pressure of argon. Stirring was commenced, and the addition *n*-butyllithium (34.4 mL, 50 mmol, 1.6 M in hexanes) in a dropwise manner *via* syringe over a period of 30 minutes was begun. After completing the addition of *n*-butyllithium the reaction was stirred for an additional 1 hour. The reaction mixture was then allowed to warm at room temperature for approximately 1 hour. After this time the reaction mixture was cooled back down to -78

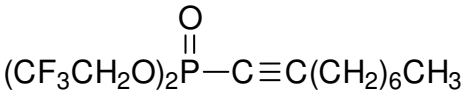
ºC and stirred for an additional 2 hours. Finally bis(2,2,2 trifluoroethyl) phosphorochloridate (9.3 mL, 56 mmol) was added dropwise *via* syringe over a period of approximately 20 minutes and the reaction mixture allowed to stir overnight. An aqueous work up was performed quenching with saturated ammonium chloride (3x50 mL) and subsequently washing with water (3x50 mL) to remove excess salts. The product was extracted into ether (3x50 mL), dried over anhydrous magnesium sulfate and filtered. The solvent was removed by rotary evaporation and fractionally distilled under high vacuum to yield compound **6** (26.3 g, 50%) as a clear colorless viscous oil.

^{31}P NMR ($CDCl_3$) δ -4.97.

^{1}H NMR ($CDCl_3$) δ 0.90 (t, *J* = 6.9, 3H), 1.44-1.36 (m, 2H), 1.35-1.26 (m, 4H), 1.58 (quintet, *J* = 7.3 Hz, 2H), 2.40 (dt, *J* = 7.2, 4.7 Hz, 2H), 4.40 (dq, *J* = 8.3, 8.0 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.28 (s), 18.92 (d, *J* = 4.8 Hz), 21.83 (s), 29.08 (d, *J* = 2.2 Hz), 62.58 (2, dq, *J* = 38.2, 4.2 Hz), 67.32 (d, *J* = 331.0 Hz), 107.19 (d, *J* = 58.8 Hz), 122.14 (2, dq, *J* = 277.0, 10.2 Hz).

Bis(2,2,2-trifluoroethyl) non-1-ynylphosphonate (7).



1-Nonyne (25 g, 33 mL, 0.2 mol) was transferred to an argon-flushed 3 liter round bottom flask containing 1200 mL 50:50 pentane and diethyl ether, and a magnetic stir bar. The reaction vessel was cooled to -78 ºC and put under the positive pressure of argon using a rubber septum and argon-filled balloon fitted to the top of the flask. Stirring was commenced, and the addition *n*-butyllithium (110 mL, 0.220 mol, 2.0 M in pentane) dropwise *via* syringe over a period of 30 minutes was begun. After the addition of *n*-butyllithium was complete the reaction was stirred for an additional 1 hour; after which

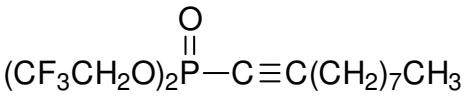
time the reaction mixture was allowed to stir at room temperature to for one hour. The reaction mixture was then cooled to -78 ºC and stirred for an additional 2 hours. Finally bis(2,2,2 trifluoroethyl) phosphorochloridate (37.2 mL, 224 mmol) was added dropwise *via* syringe over a period of approximately 30 minutes and the reaction mixture allowed to stir overnight. The reaction was quenched using saturated ammonium chloride (3x50 mL) and subsequently washed with water (3x50 mL) to remove any excess salts. The product was extracted into ether (3x50 mL), dried over anhydrous magnesium sulfate, and filtered. The solvent was removed by rotary evaporation and fractionally distilled under high vacuum to yield compound **7** (43.6 g, 59%) as a clear and colorless viscous oil.

^{31}P ($CDCl_3$) δ -5.01.

^{1}H NMR ($CDCl_3$) δ 0.85 (t, J = 6.8 Hz, 3H), 1.30-1.18 (m, 6H), 1.39-1.32 (m, 2H), 1.57 (quintet, J = 7.3 Hz, 2H), 2.36 (dt, J = 7.2, 4.7 Hz, 2H), 4.36 (dq, J = 8.4, 8.2 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 19.05 (s), 22.39 (s), 22.33 (s), 26.94 (s), 26.97 (s) 28.45 (s), 28.56 (s), 31.41 (s), 67.31 (d, J =331.5 Hz) 107.27 (d, J = 58.5 Hz), 122.25 (2, dq, J = 277.5, 9.9 Hz).

Bis(2,2,2 trifluoroethyl) dec-1-ynylphosphonate (8).



1-Decyne (25 g, 32.6 mL, 180 mmol) was transferred to an argon-flushed 3 liter round bottom flask containing 1200 mL 50:50 pentane and diethyl ether, and a magnetic stir bar. The reaction vessel was cooled to -78 ºC and put under the positive pressure of argon. The reaction mixture was stirred, and the addition *n*-butyllithium (135 mL, 216 mmol, 1.6 M in hexanes) dropwise *via* syringe over a period of 30 minutes was begun.

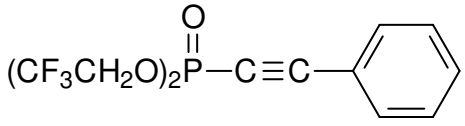
After the addition of *n*-butyllithium was complete the reaction was stirred for an additional one hour. The reaction was then stirred for a period one hour at room temperature and subsequently cooled to -78 ºC and stirred for an additional 2 hours. Finally bis(2,2,2-trifluoroethyl) phosphorochloridate (37.2 mL, 224 mmol) was added *via* syringe over a period of approximately 30 minutes and the reaction mixture allowed to stir overnight. The reaction was quenched using saturated ammonium chloride (3x50 mL) and subsequently washed with water (3x50 mL) to remove excess salts. The product was extracted with ether (3x50 mL), dried over anhydrous magnesium sulfate and subsequently filtered. The solvent was removed by rotary evaporation and fractionally distilled under high vacuum to yield compound **8** (31.9 g, 46%) as a clear and colorless viscous oil.

^{31}P ($CDCl_3$) δ -5.75.

^{1}H NMR ($CDCl_3$) δ 0.89 (t, *J* = 6.82 Hz, 3H), 1.43-1.39 (m, 2H), 1.30-1.29 (m, 8H), 1.61 (quintet, *J* = 7.3 Hz, 2H), 2.40 (dt, *J* = 7.14, 4.68 Hz, 2H), 4.40 (dq, *J* = 8.38, 7.96 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.72 (s), 19.02 (d, *J* = 4.4 Hz), 22.44 (s), 26.93 (s), 28.57 (s), 28.72 (s), 28.87 (s), 31.59 (s), 62.43 (2, dq, *J* = 38.3, 4.4 Hz), 107.11 (d, *J* = 58.5 Hz). 122.18 (2, dq, *J* = 277.4, 10.3 Hz).

Bis(2,2,2-trifluoroethyl) phenylethynylphosphonate (9).



To an argon-evacuated 500 mL round bottom flask containing a magnetic stir bar and 250 mL of ether:pentane (50:50) was added 50 mmol (5.12 g, 5.5 mL) of phenylacetylene and

50 mmol (8.96 g, 8.7 ml) hexamethylphosphoramide (HMPA). The reaction was put under the positive pressure of argon and stirring was commenced. The reaction mixture was cooled to –78 ° C and *n*-butyllithium (34.4 mL, 55 mmol, 1.6 M in hexanes) was added dropwise *via* syringe. The reaction was stirred at -78 °C for one hour and then subsequently stirred for one hour at room temperature. The reaction mixture was then cooled back down to -78 °C and stirred for an additional two hours prior to the addition of bis(2,2,2-trifluoroethyl) phosphorochloridate (56 mL) in a dropwise fashion *via* syringe. The reaction was allowed to stir overnight. Solvent was then removed through rotary evaporation and the final product isolated through fractional distillation under high vacuum to yield compound **9** (1.63 g, 10%) as a clear, colorless and viscous oil.

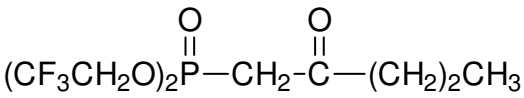
^{31}P NMR ($CDCl_3$) δ -4.42.

^{1}H NMR ($CDCl_3$) δ 2.65 (dd, J = 9.2, 0.72)

^{13}C NMR ($CDCl_3$) δ

Bis(2,2,2 trifluoroethyl) β-ketophosphonates:

Bis(2,2,2 trifluoroethyl) 2-oxopentylphosphonate(10).



To a solution of **3** (0.327 g, 1 mmol), $HgSO_4$ (0.076 g, 0.25 mmol) and 2.3 mL of 2,2,2-trifluoroethanol contained in a 50 mL round bottom flask with a magnetic stir bar was added 0.90 mL of 10% H_2SO_4. The flask was fitted with a reflux condenser and water allowed to flow. Stirring was commenced and the reaction mixture allowed to gently reflux overnight for a period of 17 hours. The reaction mixture was transferred to a separatory funnel and extracted into chloroform (3x5 mL). The organic portion was then dried over anhydrous magnesium sulfate and filtered. The chloroform was removed by

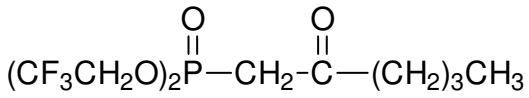
rotary evaporation and the crude product was purified *via* flash column using hexanes and ethyl acetate (80:20) to yield compound **10** (0.230 g, 66%) as a transparent viscous pale yellow oil.

^{31}P NMR ($CDCl_3$) δ 24.67.

^{1}H NMR ($CDCl_3$) δ 0.91 (t, *J* = 7.4 Hz, 3H), 1.61 (sextet, *J* = 7.3 Hz, 2H), 2.54 (t, *J* = 7.2 Hz, 2H), 3.25 (d, *J* = 21.6 Hz, 2H), 4.43 (dq, *J* = 8.3, 8.2 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.27 (s), 16.69 (d, *J* = 1.5 Hz), 40.43 (s), 41.8 (s), 46.28 (d, *J* = 5.12 Hz), 62.29 (2, dq, *J* = 38.1, 5.1 Hz), 122.45 (2, dq, *J* = 277.4, 8.0 Hz), 201.16 (d, *J* = 7.3 Hz).

Bis(2,2,2 trifluoroethyl) 2-oxohexylphosphonate (11).



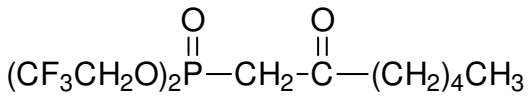
To a solution of **4** (0.336 g, 1 mmol), $HgSO_4$ (0.069 g, ~0.2 mmol) and 2.3 mL of 2,2,2-trifluoroethanol contained in a 50 mL round bottom flask with a magnetic stir bar was added 0.90 mL of 10% H_2SO_4. The flask was fitted with a reflux condenser and water allowed to flow. Stirring was commenced and the reaction mixture allowed to gently reflux overnight for a period of 17 hours. The reaction mixture was transferred to a separatory funnel and extracted into chloroform (3x5 mL). The organic portion was then dried over anhydrous magnesium sulfate and filtered. The chloroform was removed by rotary evaporation and the crude product was purified *via* flash column chromatography using hexanes:ethyl acetate (80:20) to yield compound **11** (7.05 g, 81%) as a clear transparent viscous pale yellow oil.

^{31}P NMR ($CDCl_3$) δ 24.69.

^{1}H NMR ($CDCl_3$) δ 0.87 (t, 7.3 Hz, 3H), 1.28 (sextet, *J* = 5.3 Hz, 2H), 1.53 (quintet, *J* = 7.5 Hz, 2H), 2.54 (t, 7.3 Hz, 2H), 3.24 (d, *J* = 21.6 Hz, 2H), 4.41 (dq, *J* = 8.3, 8.1 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 14.98 (s), 23.21 (s), 26.54 (d, *J* = 0.80 Hz), 42.36 (d, *J* = 138.5 Hz), 45.45 (*J* = 5.0 Hz), 63.51 (2, dq, *J* = 38.0, 5.7 Hz), 123.53 (2, dq, *J* = 277.0, 8.4 Hz), 202.26 (d, *J* = 7.0 Hz).

Bis(2,2,2-trifluoroethyl) 2-oxoheptylphosphonate (12).



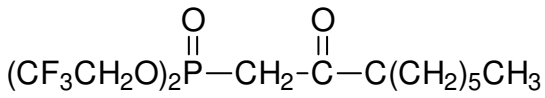
To a solution of **5** (0.385 g, 1 mmol), $HgSO_4$ (0.071 g, 0.2 mmol) and 2.3 mL of 2,2,2-trifluoroethanol contained in a 50 mL round bottom flask with a magnetic stir bar was added 0.90 mL 10% H_2SO_4. The flask was fit with a reflux condenser and water allowed to flow. Stirring was commenced and the reaction mixture allowed to gently reflux overnight for a period of 17 hours. The reaction mixture was transferred to a separatory funnel and extracted into chloroform (3x5 mL). The organic portion was then dried over anhydrous magnesium sulfate and filtered. The chloroform was removed by rotary evaporation and the crude product was purified *via* flash column chromatography using hexanes:ethyl acetate (80:20) to yield compound **12** (0.405 g, 57%) as a clear transparent viscous pale yellow oil.

^{31}P NMR ($CDCl_3$) δ 24.69.

^{1}H NMR ($CDCl_3$) δ 0.87 (t, *J* = 6.8 Hz, 3H), 1.20-1.34 (m, 4H), 1.59 (quintet, *J* = 7.4 Hz, 2H) 2.5 (t, *J*=7.3 Hz, 2H) 3.26 (d, 2H *J* = 21.6) 4.43 (dq, 4H, *J* = 8.3, 8.1 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.52 (s), 22.15 (s), 22.81 (s), 30.83 (s), 40.93 (d, *J* = 137.9 Hz), 44.25 (d, *J* = 5.13 Hz), 62.21 (2, dq, *J* = 38.0, 5.5 Hz), 122.43 (2, dq, *J* = 277.3, 8.8 Hz), 201.16 (d, *J* = 6.6 Hz).

Bis(2,2,2-trifluoroethyl) 2-oxooctyphosphonate (13).



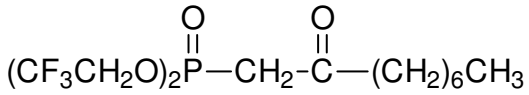
To a solution of **6** (0.365g, 1 mmol), $HgSO_4$ (0.086 g, 0.3 mmol) and 2.3 mL of 2,2,2-trifluoroethanol contained in a 50 mL round bottom flask with a magnetic stir bar was added 0.90 mL 10% H_2SO_4. The flask was fitted with a reflux condenser and water allowed to flow. Stirring was commenced and the reaction mixture allowed to gently reflux overnight for a period of 17 hours. The reaction mixture was transferred to a separatory funnel and extracted into chloroform (3x5 mL). The organic portion was then dried over anhydrous magnesium sulfate and filtered. The chloroform was removed by rotary evaporation and the crude product was purified *via* flash column using 80:20 hexanes:ethyl acetate to yield compound **13** (0.200 g, 52%) as a transparent viscous pale yellow oil.

^{31}P ($CDCl_3$) δ 24.70.

^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.22-1.34 (m, 6H), 1.53-1.60 (m, 2H), 2.55 (t, *J* = 7.3 Hz, 2H), 3.25 (d, *J* = 21.6 Hz, 2H), 4.45 (dq, *J* = 8.3, 8.1 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 15.23 (s), 23.67 (s), 24.46 (s), 29.74 (s), 32.69 (s), 43.37 (d, *J* = 5.12 Hz), 45.76 (s), 62.24 (2, dq, *J* = 38.1, 5.9 Hz), 122.45 (2, dq, *J* = 277.4, 8.0 Hz), 201.29 (d, *J* = 7.3 Hz).

Bis(2,2,2-trifluoroethyl) 2-oxononylphosphonate (14).



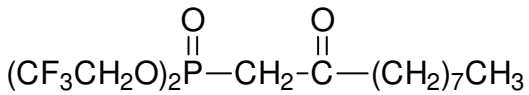
To a solution of **7** (27.62 g, 75 mmol), $HgSO_4$ (5.06 g, 17 mmol) and 172.5 mL of 2,2,2-trifluoroethanol contained in a 500 mL round bottom flask with a magnetic stir bar was added 67.5 mL of 10% H_2SO_4. The flask was fitted with a reflux condenser and water allowed to flow. Stirring was commenced and the reaction mixture allowed to gently reflux overnight for a period of 23 hours. The reaction mixture was transferred to a separatory funnel and extracted into chloroform (3x5 mL) and filtered through celite. The organic portion was then dried over anhydrous magnesium sulfate and filtered. The chloroform was removed by rotary evaporation and the crude product was purified *via* flash column using 80:20 hexanes:ethyl acetate to yield compound **14** (12.99 g, 45%) as a transparent viscous pale yellow oil.

^{31}P ($CDCl_3$) δ 24.75.

^{1}H NMR ($CDCl_3$) δ 0.86 (t, *J* = 6.9 Hz, 3H), 1.22-1.30 (m, 8H), 1.53-1.56 (m, 2H), 2.51-2.55 (t, *J* = 7.3 Hz, 2H), 3.27 (d, *J* = 21.5 Hz, 2H), 4.44 (dq, *J* = 8.3, 8.1 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.76 (s), 22.39 (s), 23.11 (s), 28.64 (s), 28.80 (s), 31.43 (s), 40.91 (d, *J* = 139.05 Hz), 44.32 (d, *J* = 5.12 Hz), 62.17 (2, dq, *J* = 38.1, 5.9 Hz), 122.44 (2, dq, *J* = 277.2, 8.4 Hz), 201.24 (d, *J* = 7.3 Hz).

Bis(2,2,2-trifluoroethyl) 2-oxodecylphosphonate (15).



To a solution of **8** (28.67 g, 75 mmol), $HgSO_4$ (5.06 g, 17 mmol) and 172.5 mL of 2,2,2-trifluoroethanol contained in a 500 mL round bottom flask with a magnetic stir bar was

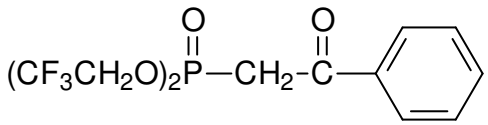
added 67.5 mL 10% H_2SO_4. The flask was fitted with a reflux condenser and water allowed to flow. Stirring was commenced and the reaction mixture allowed to gently reflux overnight for a period of 21 hours. The reaction mixture was transferred to a separatory funnel and extracted into chloroform (3x5 mL) and filtered through celite. The organic portion was then dried over anhydrous magnesium sulfate and filtered. The chloroform was removed by rotary evaporation and the crude product was purified *via* flash column using 80:20 hexanes:ethyl acetate to yield compound **15** (13.94 g, 46%) as a transparent viscous pale yellow oil.

^{31}P NMR ($CDCl_3$) δ 24.75.

^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 6.9 Hz, 3H), 1.27-1.32 (m, 10H), 1.57-1.60 (m, 2H), 2.57 (t, *J* = 7.32 Hz, 2H), 4.45 (dq, *J* = 8.3, 8.1 Hz, 4H).

^{13}C NMR ($CDCl_3$) δ 13.95 (s), 22.54 (s), 23.20 (s), 28.78 (s), 28.99 (s), 29.18 (s), 31.70 (s), 41.05 (d, *J* = 138.31 Hz), 44.46 (d, *J* = 5.1 Hz), 62.28 (2, dq, *J* = 38.1, 5.1 Hz), 122.42 (2, dq, *J* = 277.4, 8.8 Hz), 201.29 (d, *J* = 6.6 Hz).

Bis(2,2,2-trifluoroethyl) 2-oxo-2-phenylethylphosphonate (16)



To a To a solution of **9** (1.84 g, 5 mmol), $HgSO_4$ (0.371 g, 1.25 mmol) and 11.5 mL of 2,2,2-trifluoroethanol contained in a 50 mL round bottom flask with a magnetic stir bar was added 4.5 mL of 10% H_2SO_4. The flask was fitted with a reflux condenser, and stirring was commenced. The reaction mixture was allowed to gently reflux overnight for a period of 16 hours. After completion the reaction mixture was washed with a 1 M potassium iodide solution (20 mL) and transferred to a separatory funnel. The product

was extracted into chloroform (3x5 mL), and the organic portion was dried over anhydrous magnesium sulfate and filtered. The chloroform was removed by rotary evaporation and the crude product was purified *via* flash column using an 80:20 mixture of hexanes to ethyl acetate to yield compound **16** (0.20 g, 23%) as a transparent viscous pale yellow oil.

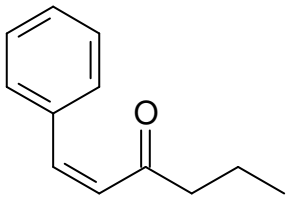
^{31}P NMR ($CDCl_3$) δ 24.90

^{1}H NMR ($CDCl_3$) δ 3.82 (d, *J* = 21.09 Hz, 2H), 4.39-4.56 (m, 4H), 7.45-7.50 (m, 2H), 7.59-7.63 (m, 1H), 7.90-7.93 (m, 2H).

^{13}C NMR δ 37.60 (d, *J* = 144.48 Hz), 62.37 (2, dq, *J* = 38.02, 5.50 Hz), 122.53 (2, dq, *J* = 277.30, 8.80 Hz), 128.65 (s), 128.88 (s), 134.37 (s), 135.69 (d, *J* = 6.60 Hz), 191.34 (d, *J* = 6.60 Hz).

Still-Gennari Horner-Wadsworth-Emmons Reactions:

(*Z*)-1-Phenyl-1-hexen-3-one (17).



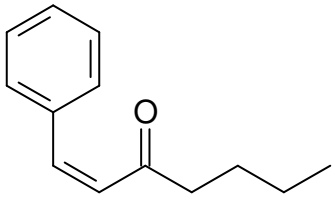
To a -78 °C stirred solution of bis(2,2,2-trifluoroethyl) pentynyl β-ketophosphonate (compound **10**, 0.330 g 1 mmol), and 18-crown-6 (1.32 g, 5 mmol) in 20 mL THF under an atmosphere of argon was added $KN(TMDS)_2$ (0.5 M in toluene, 1.51 mL, 1 mmol) in a dropwise fashion. The reaction mixture was stirred for an additional 30 minutes after which time benzaldehyde was added dropwise *via* syringe (0.1 mL, 1 mmol). The reaction mixture was stirred for 30 minutes prior to quenching with saturated ammonium chloride. The product was extracted into ether. The extracted product was washed with a

portion of water to remove residual salts. All aqueous layers were then combined and extracted with ether (3x50 mL). The ether extracts were dried over $MgSO_4$ and the solvent removed by rotary evaporation. Finally the product was purified through flash column chromatography using hexanes:ethyl acetate 80:20 to yield **16** (0.150 g, 86 %) as a viscous yellow oil.

^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.5 Hz, 3H), 1.54-1.63 (m, *J* = 7.4 Hz, 2H), 2.43 (t, *J* = 7.3 Hz, 2H), 6.18 (d, *J* = 12.9 Hz, 1H) 6.82 (d, *J* = 12.9 Hz 1H), 7.32-7.37 (m, 3H), 7.51-7.54 (m, 2H).

^{13}C NMR ($CDCl_3$) δ 13.64 (s), 17.54 (s), 30.26 (s), 45.45 (s), 128.19 (s), 128.58 (s), 129.49 (s), 135.27 (s), 139.55 (s), 203.63 (s).

(*Z*)-1-Phenyl-1-hepten-3-one (18).



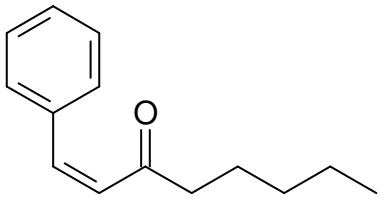
To a -78 °C stirred solution of bis(2,2,2-trifluoroethyl) hexynyl β-ketophosphonate (compound **11**, 0.414 g, 1 mmol), and 18-crown-6 (1.32 g, 5 mmol) in 20 mL THF under an atmosphere of argon was added $KN(TMDS)_2$ (0.5 M in toluene, 1.51 mL, 1 mmol) in a dropwise fashion. The reaction mixture was stirred for an additional 30 minutes after which time benzaldehyde was added dropwise *via* syringe (0.1 mL, 1 mmol). The reaction mixture was stirred for 30-60 minutes. The reaction mixture was then quenched with saturated ammonium chloride and the product extracted into ether. The extracted product was washed with a portion of water to remove any residual salts. All aqueous layers were combined and extracted with ether (3x50 mL). The ether extracts were dried

over $MgSO_4$ and the solvent removed by rotary evaporation. Finally the product was purified through flash column chromatography using hexanes:ethyl acetate 80:20 to yield **17** (0.100 g, 53 %) as a transparent viscous yellow oil.

^{1}H NMR ($CDCl_3$) δ 0.86 (t, *J* = 7.3 Hz, 3H), 1.22-1.31 (m, *J* = 7.4 Hz, 2H), 1.52-1.60 (m, *J* = 7.5 Hz, 2H), 2.44 (t, *J* = 7.44 Hz, 2H), 6.17 (d, 12.8 Hz, 1H) 6.81 (d, *J* = 12.72 Hz, 1H) 7.32-7.34 (m, 3H), 7.50-7.53 (m, 2H).

^{13}C NMR ($CDCl_3$) δ 13.78 (s), 22.16 (s), 26.18 (s), 43.23 (s), 128.14 (s), 128.54 (s), 129.01 (s), 129.44 (s), 135.25 (s), 139.50 (s), 203.45 (s).

(*Z*)-1-Phenyl-1-octen-3-one (19).



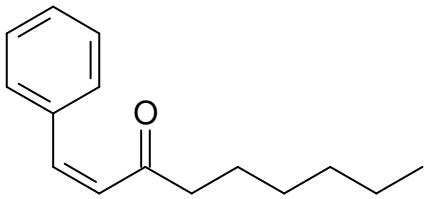
To a -78 °C stirred solution of bis(2,2,2-trifluoroethyl) heptynyl β-ketophosphonate (compound **12**, 0.358 g, 1 mmol), and 18-crown-6 (1.32 g, 5 mmol) in 20 mL THF under an atmosphere of argon was added $KN(TMDS)_2$ (0.5 M in toluene, 1.51 mL, 1 mmol) in a dropwise fashion. The reaction mixture was stirred for an additional 30 minutes after which time benzaldehyde was added dropwise *via* syringe (0.1 mL, 1 mmol). The reaction mixture was stirred for 30-60 minutes. The reaction mixture was then quenched with saturated ammonium chloride and the product extracted into ether. The extracted product was washed with a portion of water to remove any residual salts. All aqueous layers were combined and extracted with ether (3x50 mL). The ether extracts were dried over $MgSO_4$ and the solvent removed by rotary evaporation. Finally the product was

purified through flash column chromatography utilizing hexanes:ethyl acetate 80:20 to yield **18** (0.180 g, 89 %) as a viscous pale yellow oil.

^{1}H NMR ($CDCl_3$) δ 0.86 (t, *J* = 7.1 Hz, 3H), 1.17-1.31 (m, 4H), 1.54-1.61 (m, *J* = 7.5 Hz, 2H) 2.43 (t, *J* =7.4 Hz, 2H), 6.17 (d, *J* = 12.6 Hz, 1H) 6.80 (d, *J* = 12.7 Hz, 1H), 7.30-7.36 (m, 3H), 7.51-7.53 (m, 2H).

^{13}C NMR ($CDCl_3$) δ 13.80 (s), 22.31 (s), 23.72 (s), 31.17 (s), 43.44 (s), 128.08 (s), 128.48 (s), 128.96 (s), 129.41 (s), 135.20 (s), 139.44 (s), 203.34 (s).

(*Z*)-1-Phenyl-1-nonen-3-one (20).

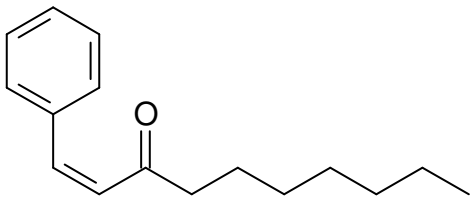


To a -78 °C stirred solution of bis(2,2,2-trifluoroethyl) octynyl β-ketophosphonate (compound **13**, 0.372, 1 mmol), and 18-crown-6 (1.32 g, 5 mmol) in 20 mL THF under an atmosphere of argon was added $KN(TMDS)_2$ (0.5 M in toluene, 1.51 mL, 1 mmol) in a dropwise fashion. The reaction mixture was stirred for an additional 30 minutes after which time benzaldehyde was added dropwise through syringe (0.1 mL, 1 mmol). The reaction mixture was stirred for 30-60 minutes. The reaction mixture was then quenched with saturated NH_4Cl and the product extracted into ether. The extracted product was washed with a portion of water to remove any residual salts. All aqueous layers were combined and extracted with ether (3x50 mL). The ether extracts were dried over $MgSO_4$ and the solvent removed by rotary evaporation. Finally the product was purified *via* flash column chromatography using hexanes:ethyl acetate 80:20 to yield **19** (0.170g, 79 %) transparent viscous yellow oil.

^{1}H NMR ($CDCl_3$) δ 0.85 (t, *J* = 6.8 Hz, 3H), 1.19-1.31 (m, 6H), 1.52-1.60 (m, *J* = 7.4 Hz, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 6.18 (d, *J* = 12.9 Hz, 1H), 6.8 (d, *J* = 12.6 Hz, 1H), 7.31-7.36 (m, 3H), 7.50-7.53 (m, 2H).

^{13}C NMR ($CDCl_3$) δ 13.97 (s), 22.41 (s), 24.06 (s), 28.73 (s), 31.51 (s), 43.55 (s), 128.16 (s), 128.58 (s), 129.02 (s), 129.45 (s), 139.49 (s), 203.51 (s).

(*Z*)-1-phenyl-1-decen-3-one (21).

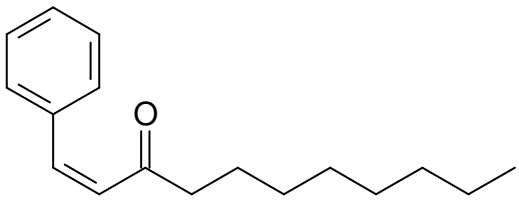


To a -78 °C stirred solution of bis(2,2,2-trifluoroethyl) nonynyl β-ketophosphonate (compound **14**, 0.230 g, 1 mmol), and 18-crown-6 (1.32 g, 5 mmol) in 20 mL THF under an atmosphere of argon was added $KN(TMDS)_2$ (0.5 M in toluene, 1.51 mL, 1 mmol) in a dropwise fashion. The reaction mixture was stirred for an additional 30 minutes after which time benzaldehyde was added dropwise *via* syringe (0.1 mL, 1 mmol). The reaction mixture was stirred for 30-60 minutes. The reaction mixture was then quenched with saturated NH_4Cl and the product extracted into ether. The extracted product was washed with a portion of water to remove any residual salts. All aqueous layers were combined and extracted with ether (3x50 mL). The ether extracts were dried over $MgSO_4$ and the solvent removed by rotary evaporation. Finally the product was purified through flash column chromatography using hexanes:ethyl acetate 80:20 to yield **20** (0.158 g, 69 %) as a transparent viscous yellow oil.

^{1}H NMR ($CDCl_3$) δ 0.86 (t, *J* = 6.9 Hz, 3H), 1.23-1.29 (m, 8H), 1.56-1.63 (m, *J* = 7.2 Hz, 2H), 2.43 (t, *J* = 7.46 Hz, 2H), 6.18 (d, *J* = 12.9 Hz, 1H), 6.81 (d, *J* = 12.6 Hz, 1H), 7.31-7.37 (m, 3H), 7.50-7.53 (m, 2H).

^{13}C NMR ($CDCl_3$) δ 14.01 (s), 22.54 (s), 24.11 (s), 29.02 (s), 30.25 (s), 31.59 (s), 43.56 (s), 128.17 (s), 128.60 (s), 129.03 (s), 129.45 (s), 135.28 (s), 139.49 (s), 203.54 (s).

(*Z*)-1-phenyl-1-undecen-3-one (22).



To a -78 °C stirred solution of bis(2,2,2-trifluoroethyl) decynyl β-ketophosphonate (compound **15**, 0.459 g, 1 mmol) 18-crown-6 (1.32 g, 5 mmol) in 20 mL THF under an atmosphere of argon was added $KN(TMDS)_2$ (0.5 M in toluene, 1.51 mL, 1 mmol) in a dropwise fashion. The reaction mixture was stirred for an additional 30 minutes after which time benzaldehyde was added dropwise *via* syringe (0.1 ml, 1 mmol). The reaction mixture was stirred for 30-60 minutes. The reaction mixture was then quenched with saturated ammonium chloride and the product extracted into ether. The extracted product was washed with a portion of water to remove any residual salts. All aqueous layers were combined and extracted with ether (3x50 mL). The ether extracts were dried over $MgSO_4$ and the solvent removed by rotary evaporation. Finally the product was purified *via* flash column chromatography using hexanes and ethyl acetate in an 80:20 ratio to yield compound **21** (0.230 g, 94 %).

^{1}H NMR ($CDCl_3$) δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.23-1.29 (m, 10H), 1.57-1.59 (m, *J* = 7.2 Hz, 2H), 2.44 (t, *J* = 7.5 Hz, 2H), 6.18 (d, *J* = 12.9 Hz, 1H), 6.8 (d, *J* = 12.9 Hz, 1H), 7.31-7.37 (m, 3H), 7.51-7.53 (m, 2H).

^{13}C NMR ($CDCl_3$) δ 13.98 (s), 22.52 (s), 24.02 (s), 29.00 (s), 29.22 (s), 31.69 (s), 43.48 (s), 125.20 (s), 128.07 (s), 128.48 (s), 128.95 (s), 129.41 (s), 135.19 (s), 139.42 (s), 203.31 (s).

Attempted Syntheses of Terminal Alkynes

3-Phenyl-1-propyne (23).

Sodium acetylide (0.25 mol, 78.68 mL, 18 wt % slurry in xylenes/light mineral oil, 95%) was suspended in 400 mL of solvent (44% DMF in xylenes) contained within a one liter three necked flask equipped with a dropping funnel, reflux condenser, and thermometer. The dropping funnel was charged with Benzyl chloride (0.25 mol, 28.82 mL). This mixture was heated to 25-30 °C. The contents of the addition funnel were discharged over a period of 20 minutes and the reaction stirred overnight. (0% yield of the desired product). Solid crystals determined to be 2,5-dibenzyl-1,2,5,6-tetraphenyl-3-hexyne were isolated (2.82 g, 12%).

3-Phenyl-1-propyne (23).

Sodium acetylide (11 mmol, 0.556 g, 3.66 mL, 18 wt % slurry in xylenes/light mineral oil, 95%) was suspended in 15 mL of THF contained in a 100 mL round bottom flask with magnetic stir bar. The neck of the flask was fitted with a condenser which in turn was equipped with an addition funnel with pressure equalizing arm. The addition funnel was charged with benzyl chloride (10 mmol, 1.39 g, 99% purity) in 10 mL of THF. The

contents were discharged dropwise. The reaction was heated to a gentle reflux and stirred overnight. The reaction was then quenched with saturated ammonium chloride. All aqueous portions were combined and extracted with ether (3x20 mL). The organic layers were dried over magnesium sulfate and the solvent removed by rotary evaporation (0% isolated yield).

5-Phenyl-1-pentyne (24).

Sodium acetylide (11 mmol, 0.556 g, 3.66 mL, 18 wt % slurry in xylenes/light mineral oil, 95%) was suspended in 15 mL of THF contained in a 100 mL round bottom flask with magnetic stir bar. The neck of the flask was fitted with a condenser which in turn was equipped with an addition funnel with pressure equalizing arm. The addition funnel was charged with 1-bromo-3-phenyl-propane (10 mmol, 1.39 g, 99% purity) in 10 mL of THF. The contents were discharged dropwise. The reaction was heated to a gentle reflux and stirred overnight. The reaction was quenched with saturated ammonium chloride (3x50 mL). All aqueous portions were combined and extracted with ether (3x50 mL). The organic layers were dried over magnesium sulfate and the solvent removed by rotary evaporation (0% yield).

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Figure 8 **^{1}H NMR of Compound 3**

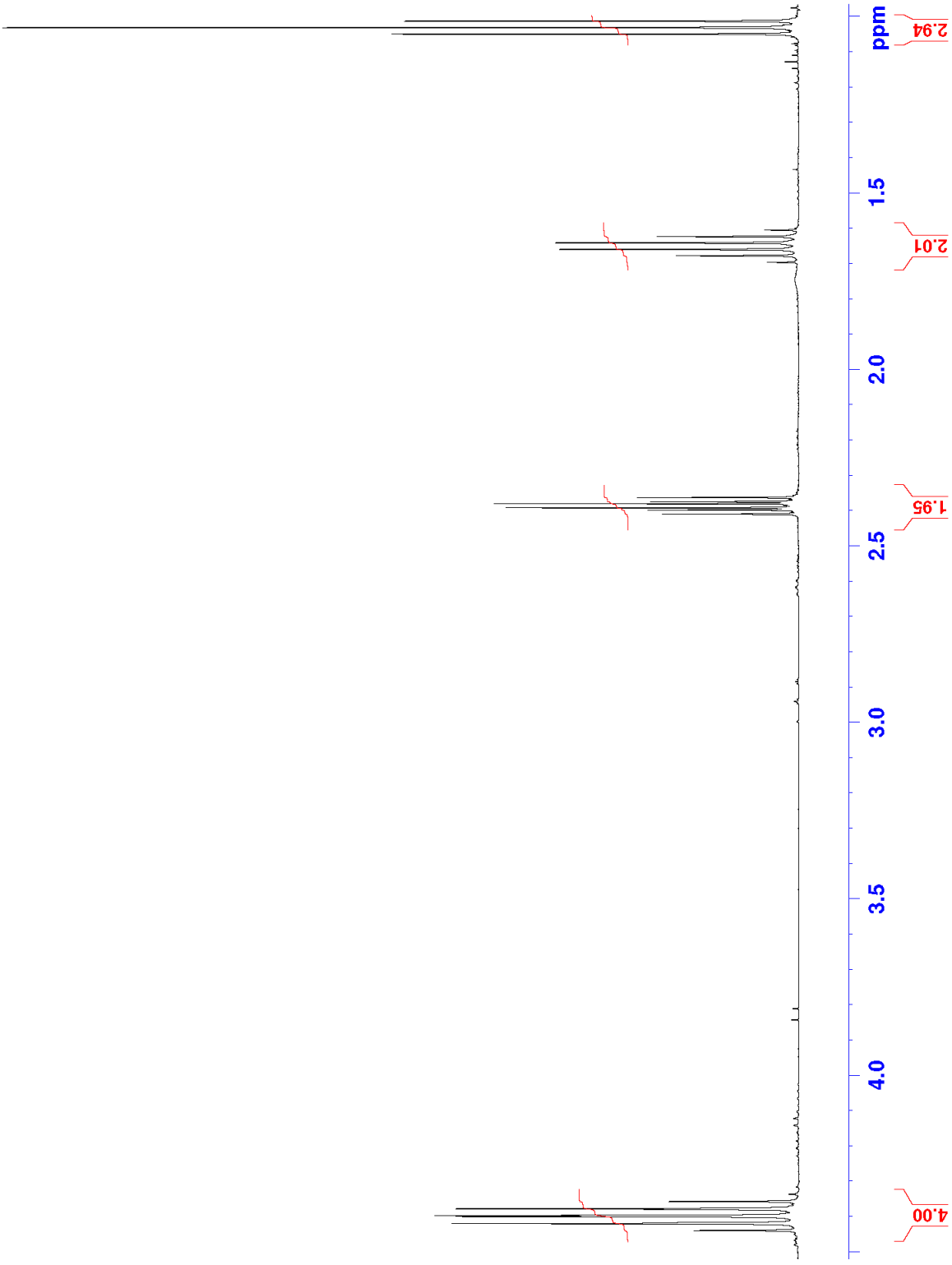


Figure 9 **^{13}C NMR of Compound 3**

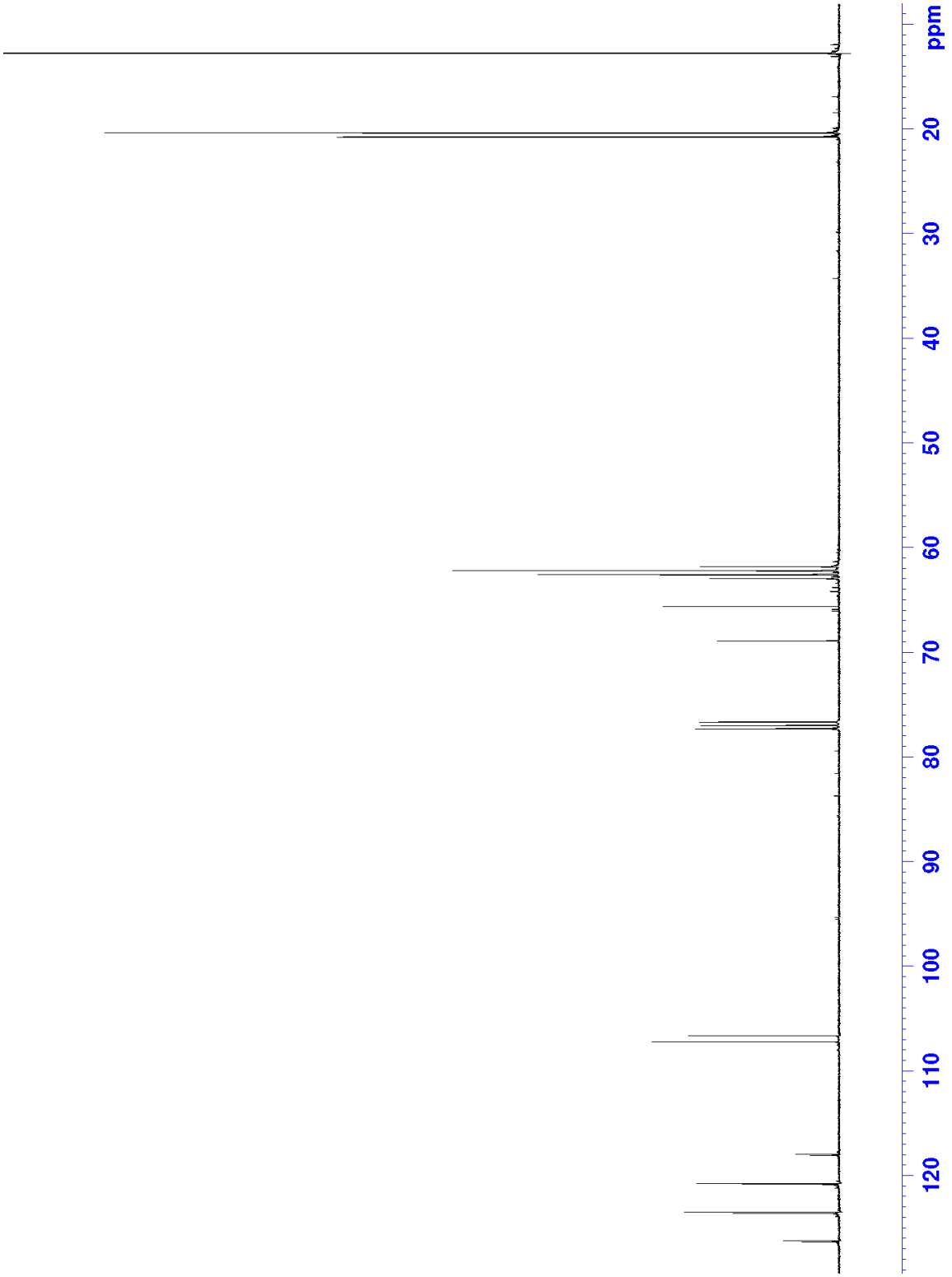


Figure 10 **^{31}P NMR of Compound 3**

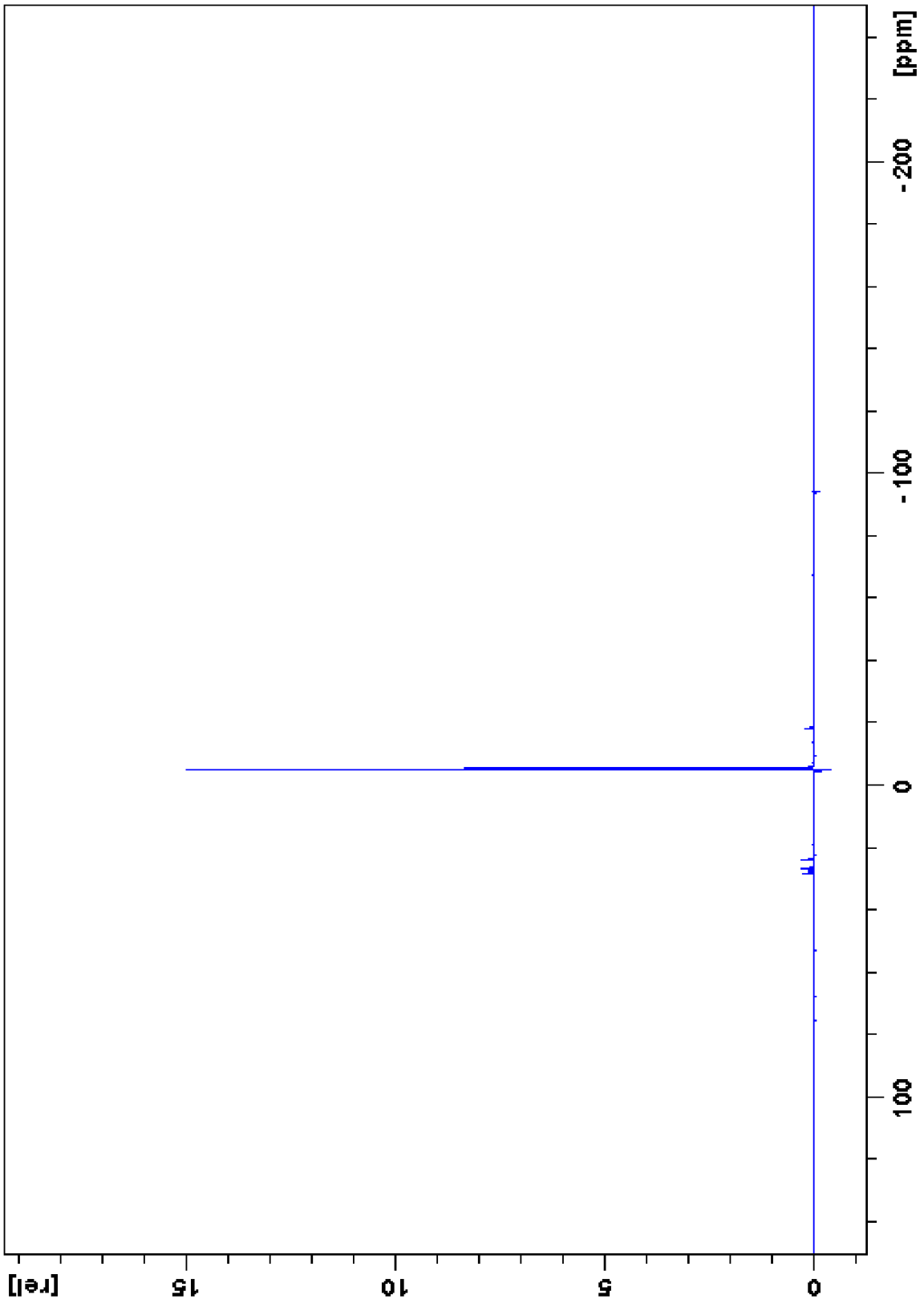


Figure 11 **^{1}H NMR of Compound 4**

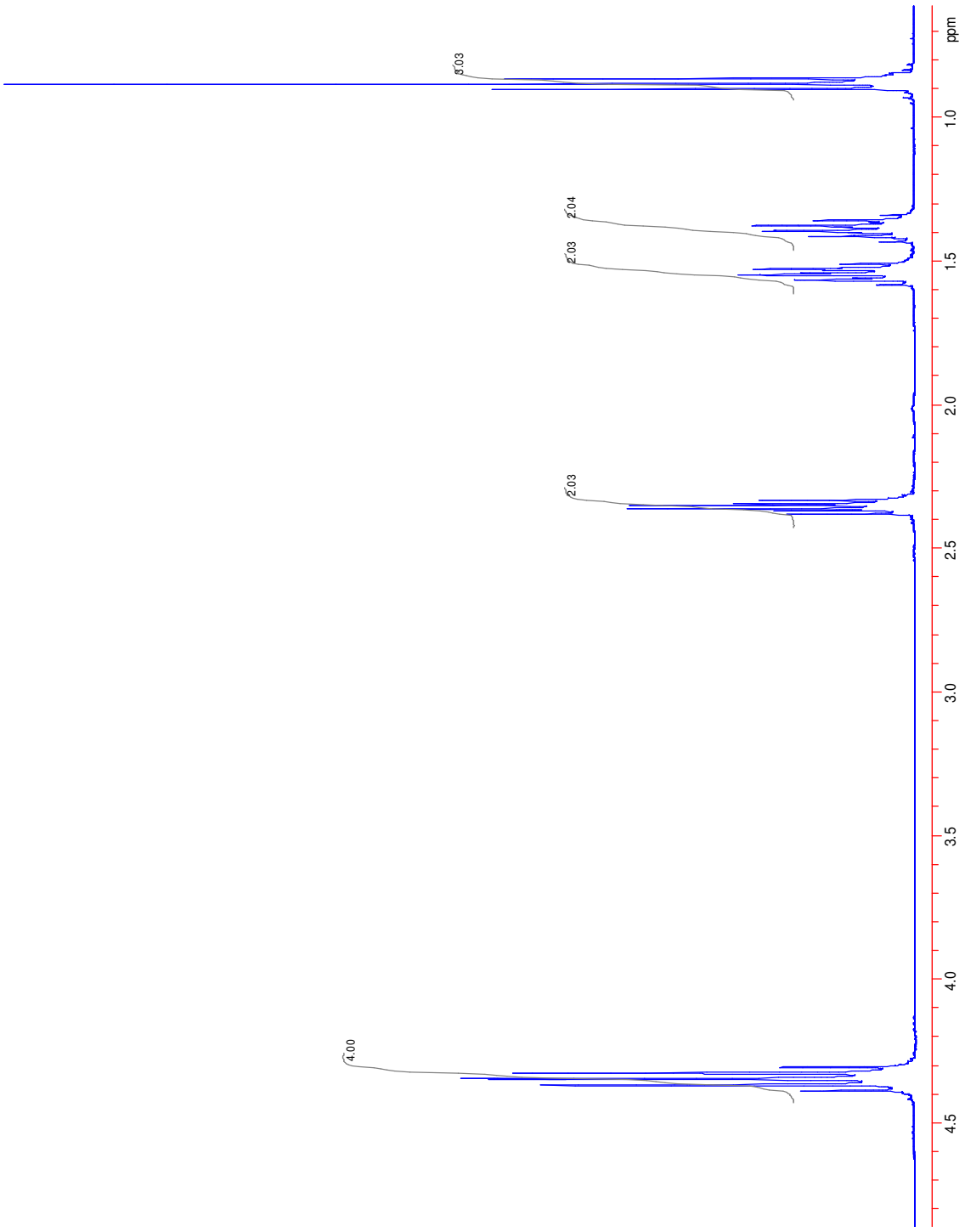


Figure 12 **^{13}C NMR of Compound 4**

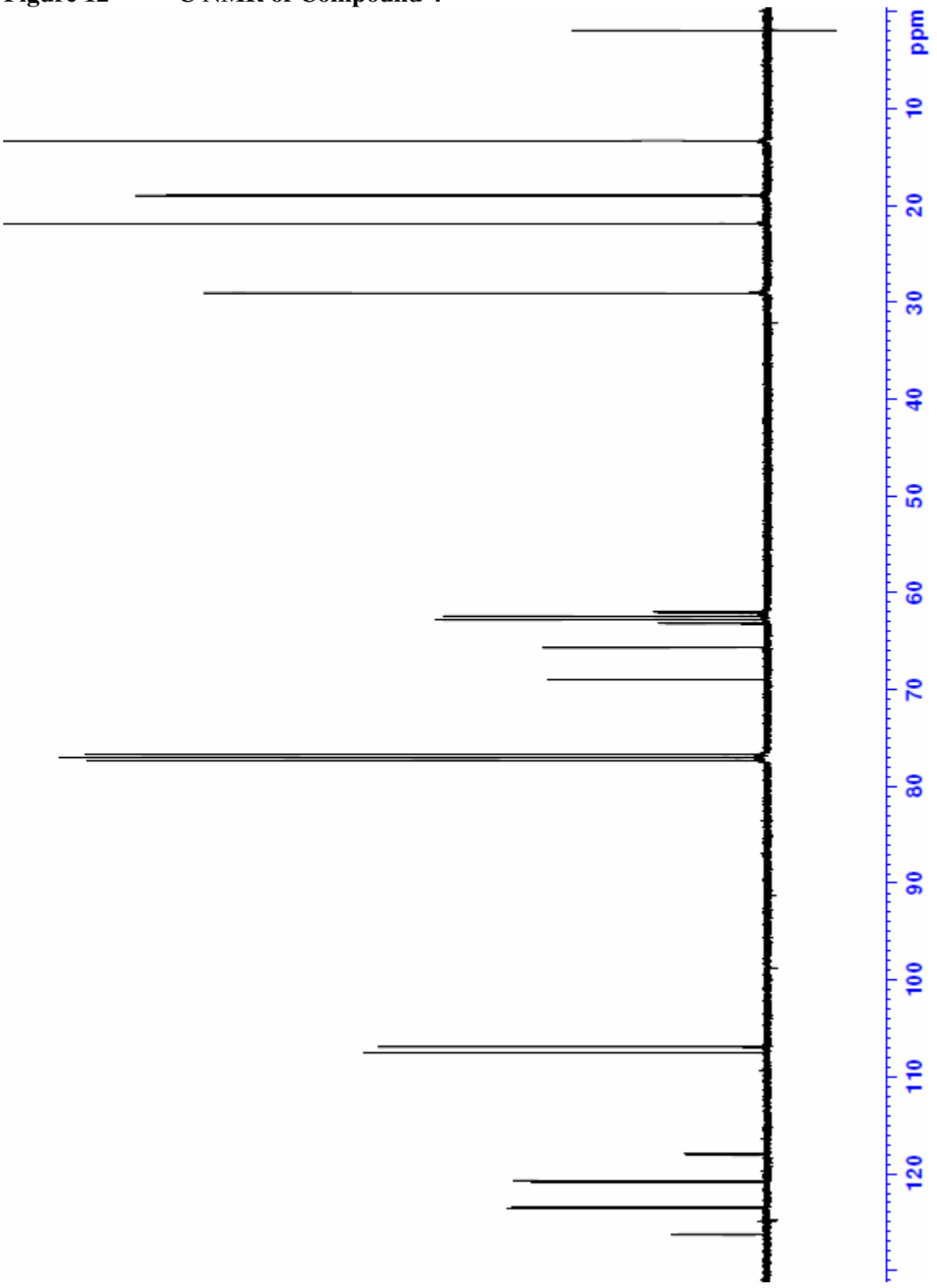


Figure 13 **^{31}P NMR of Compound 4**

Figure 14 **^{1}H NMR of Compound 5**

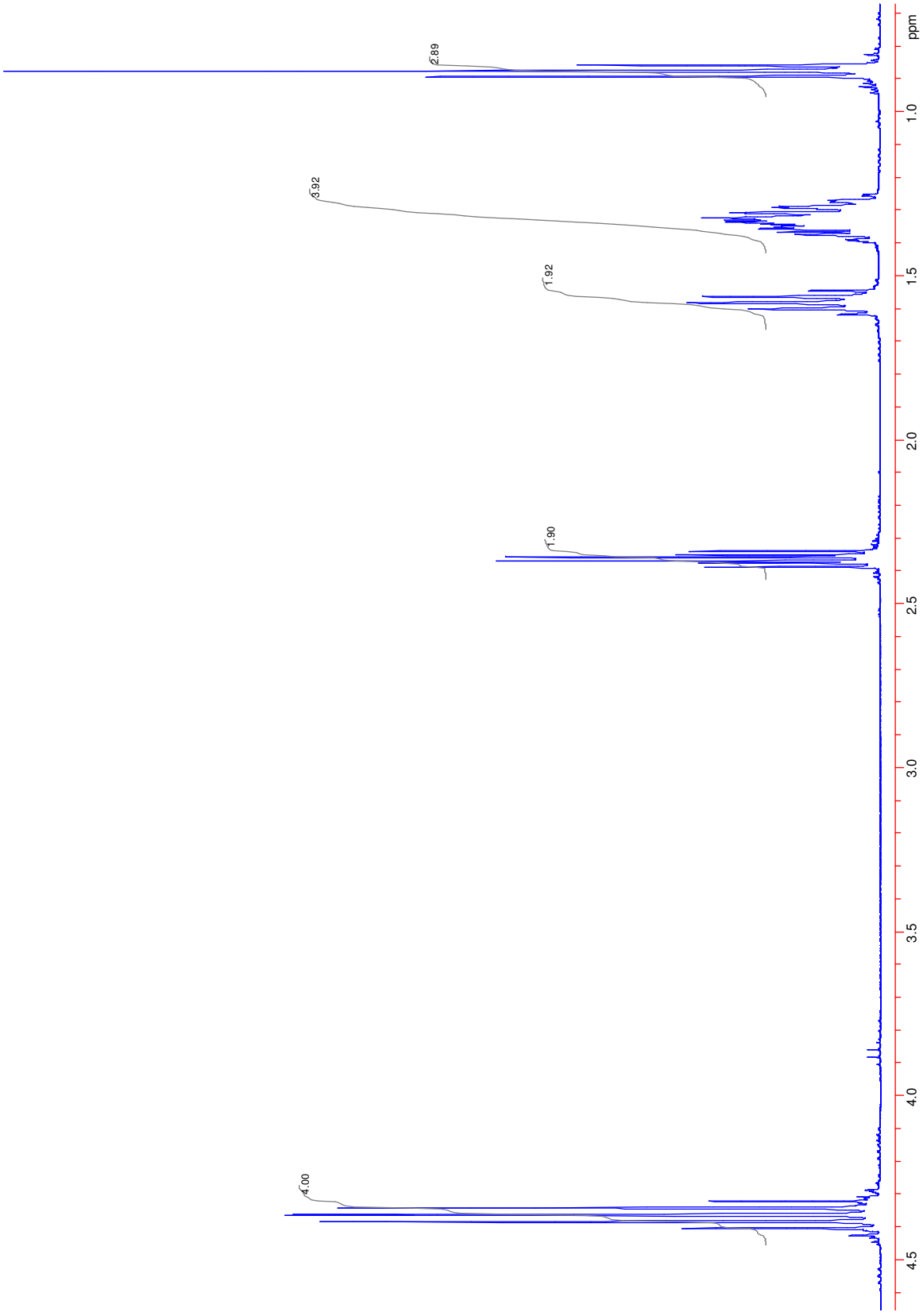


Figure 15 **^{13}C NMR of Compound 5**

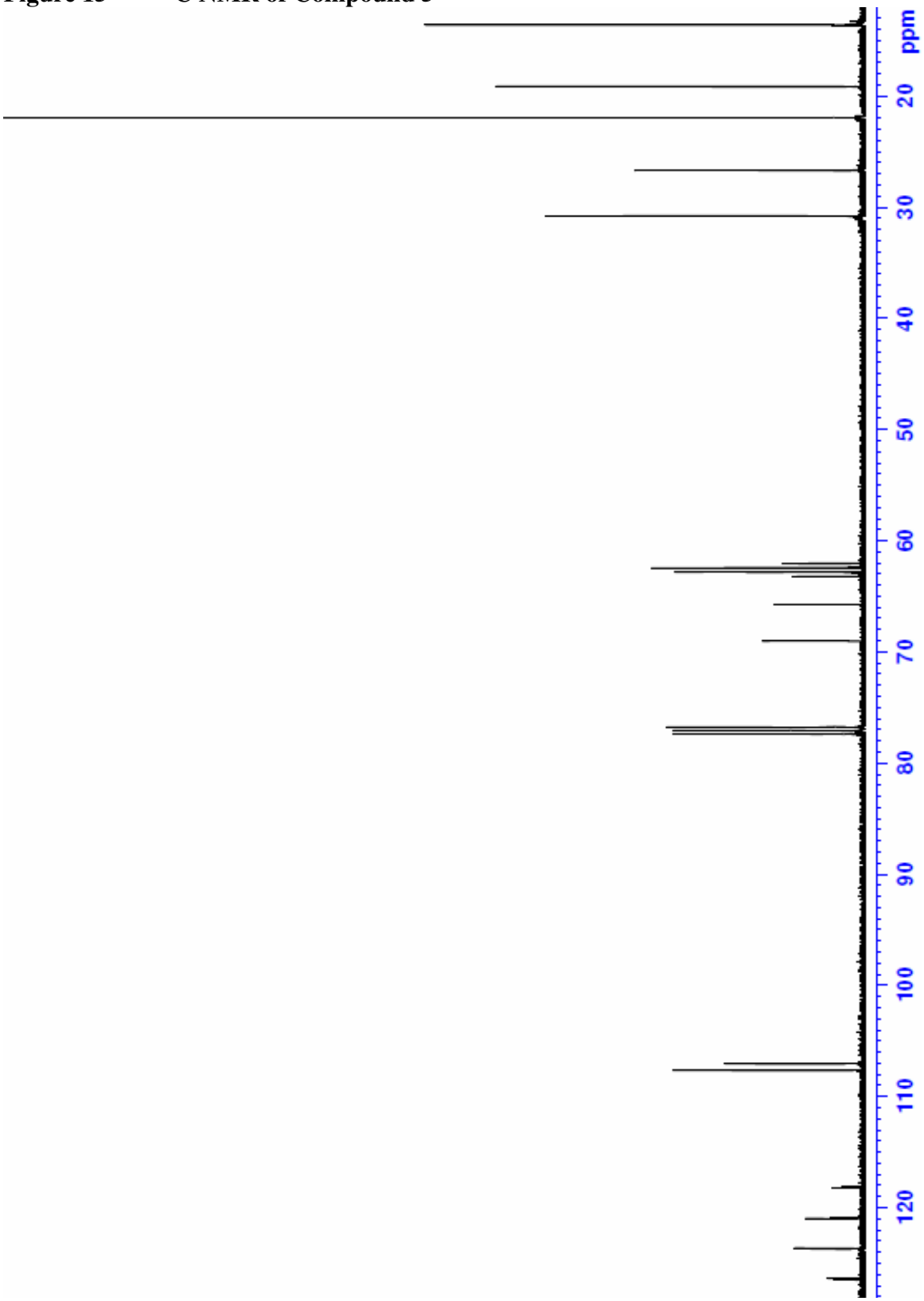


Figure 16 ^{31}**P NMR of Compound 5**

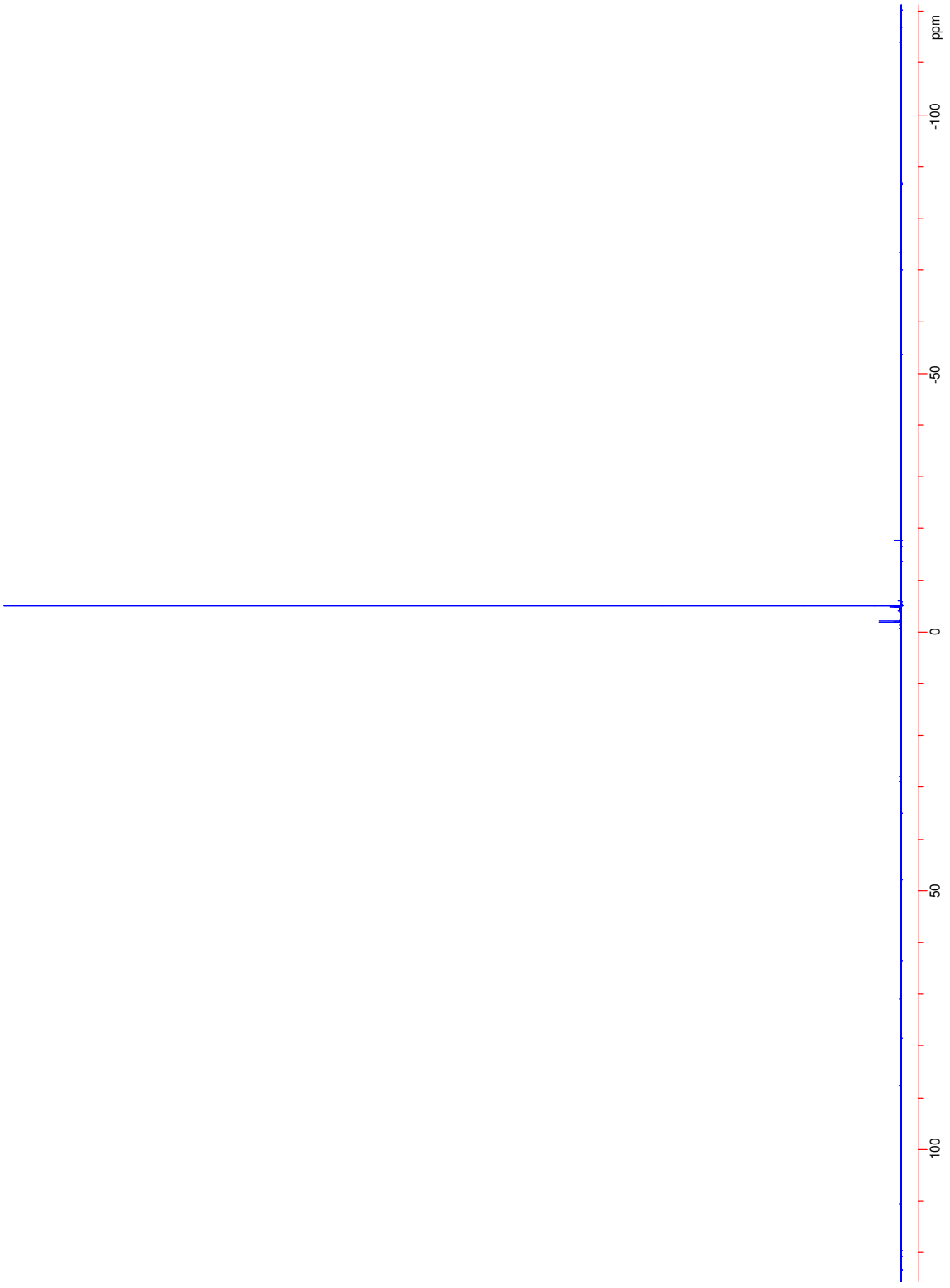


Figure 17 **^{1}H NMR of Compound 6**

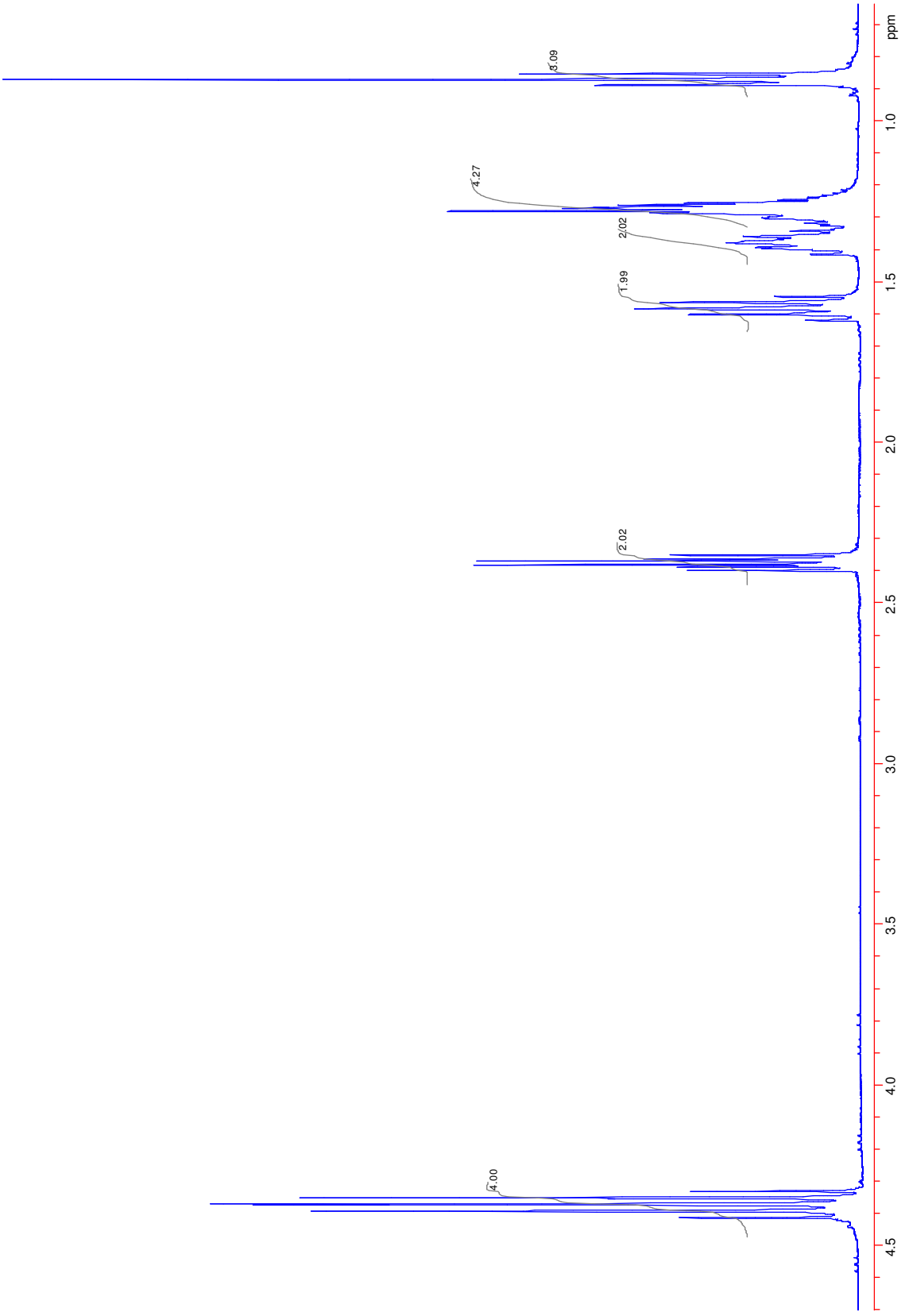


Figure 18 ^{13}C NMR of Compound 6

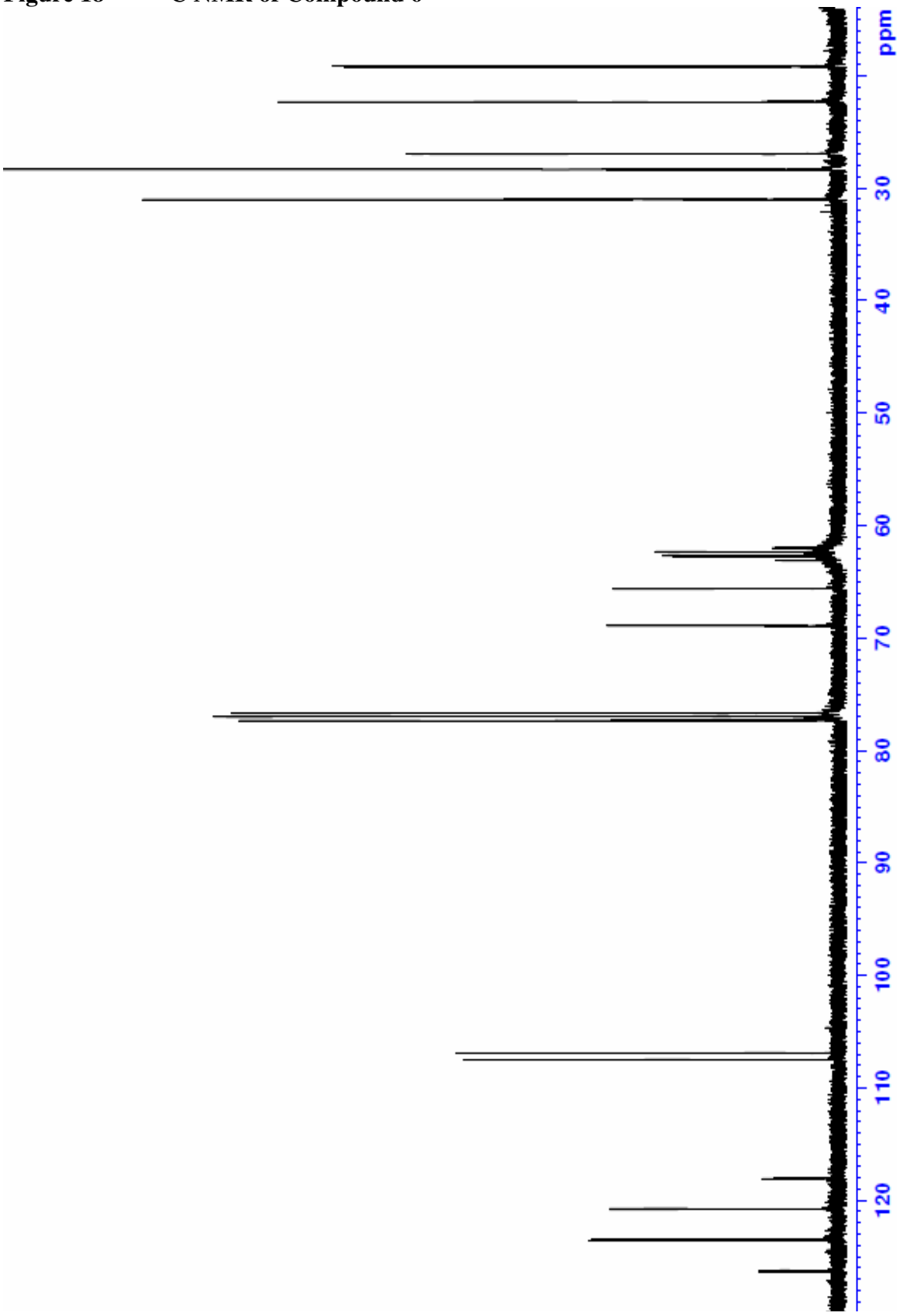


Figure 19 ^{31}**P NMR of Compound 6**

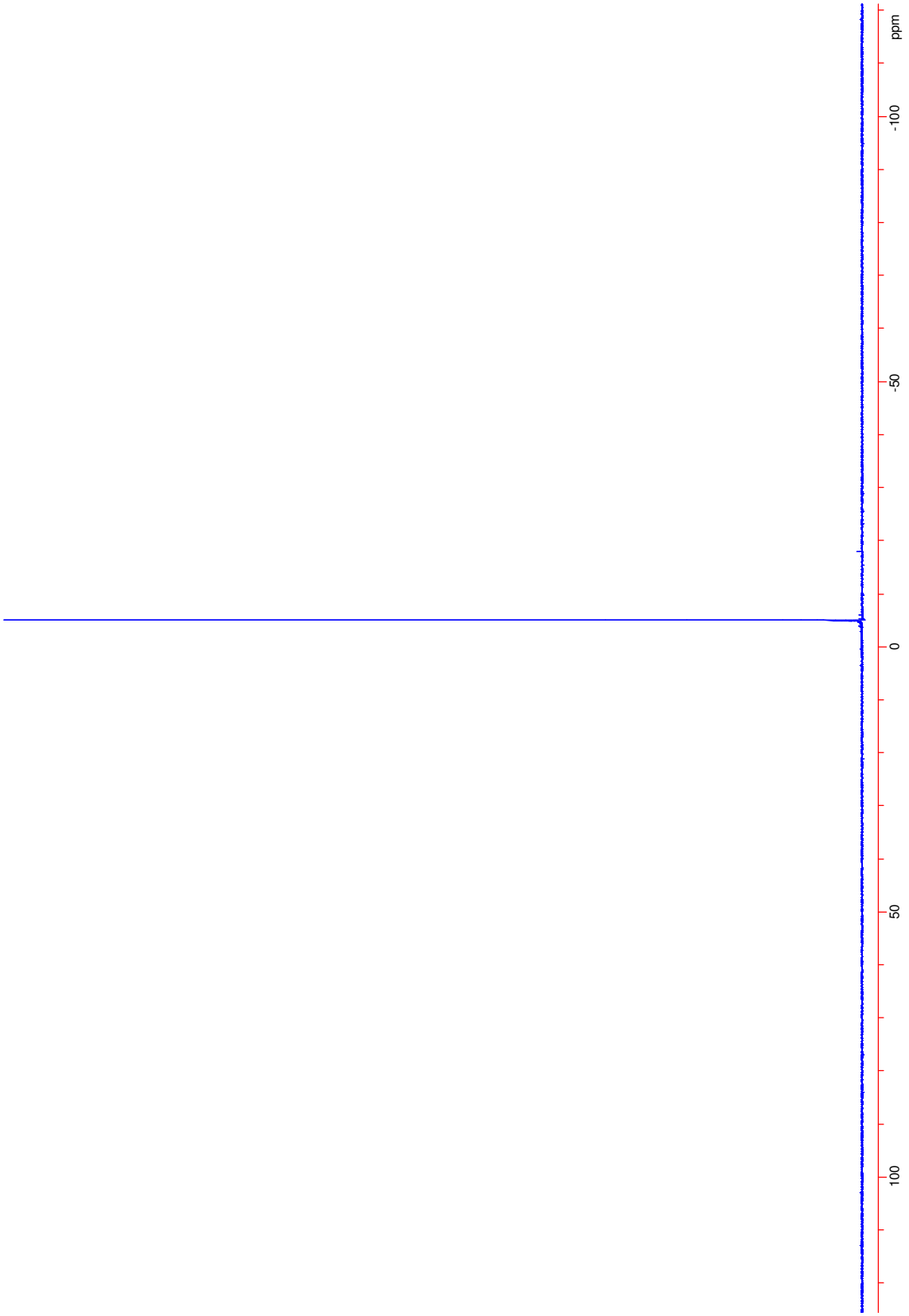


Figure 20 **^{1}H NMR of Compound 7**

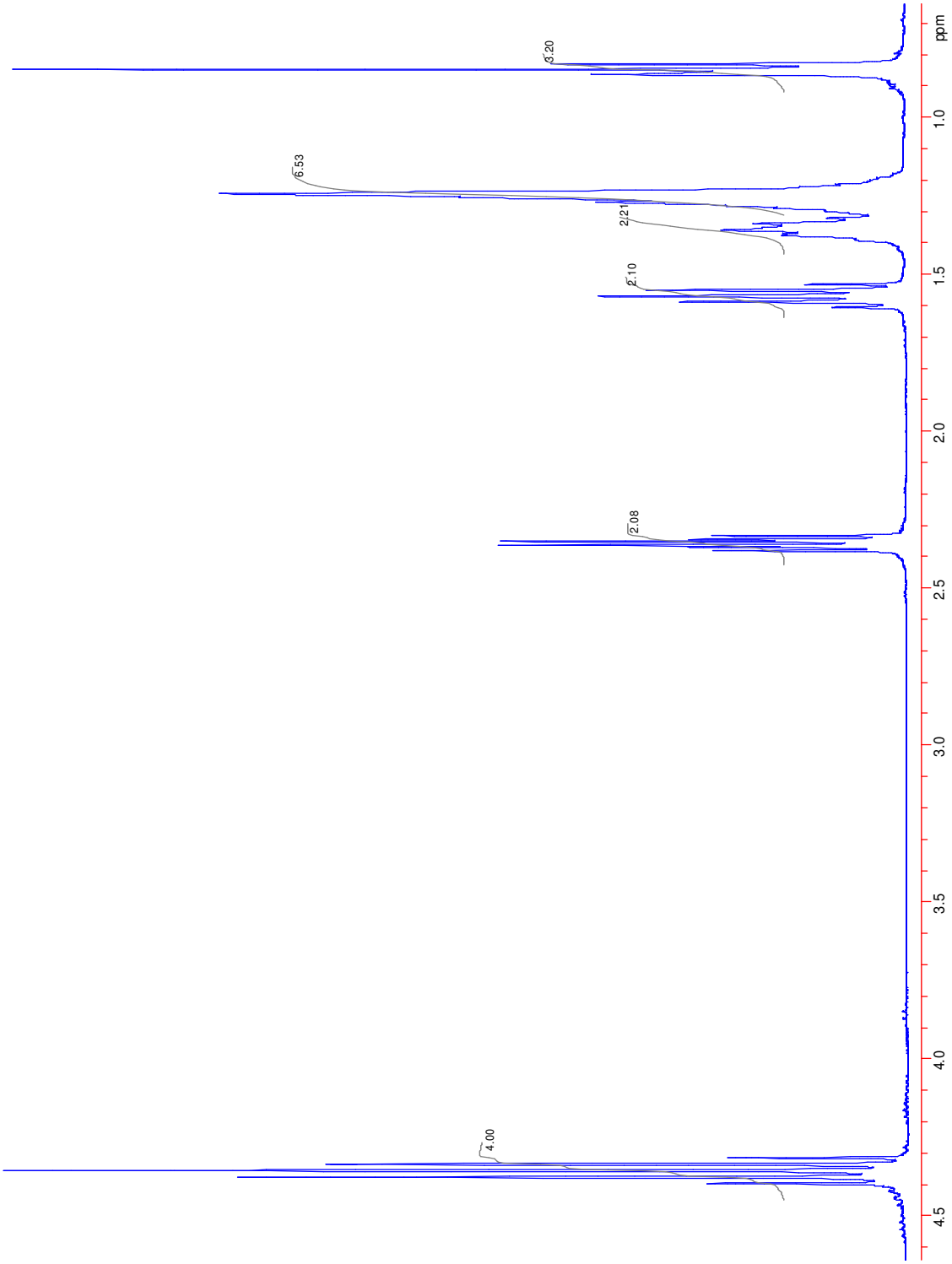


Figure 21 ^{13}C NMR of Compound 7

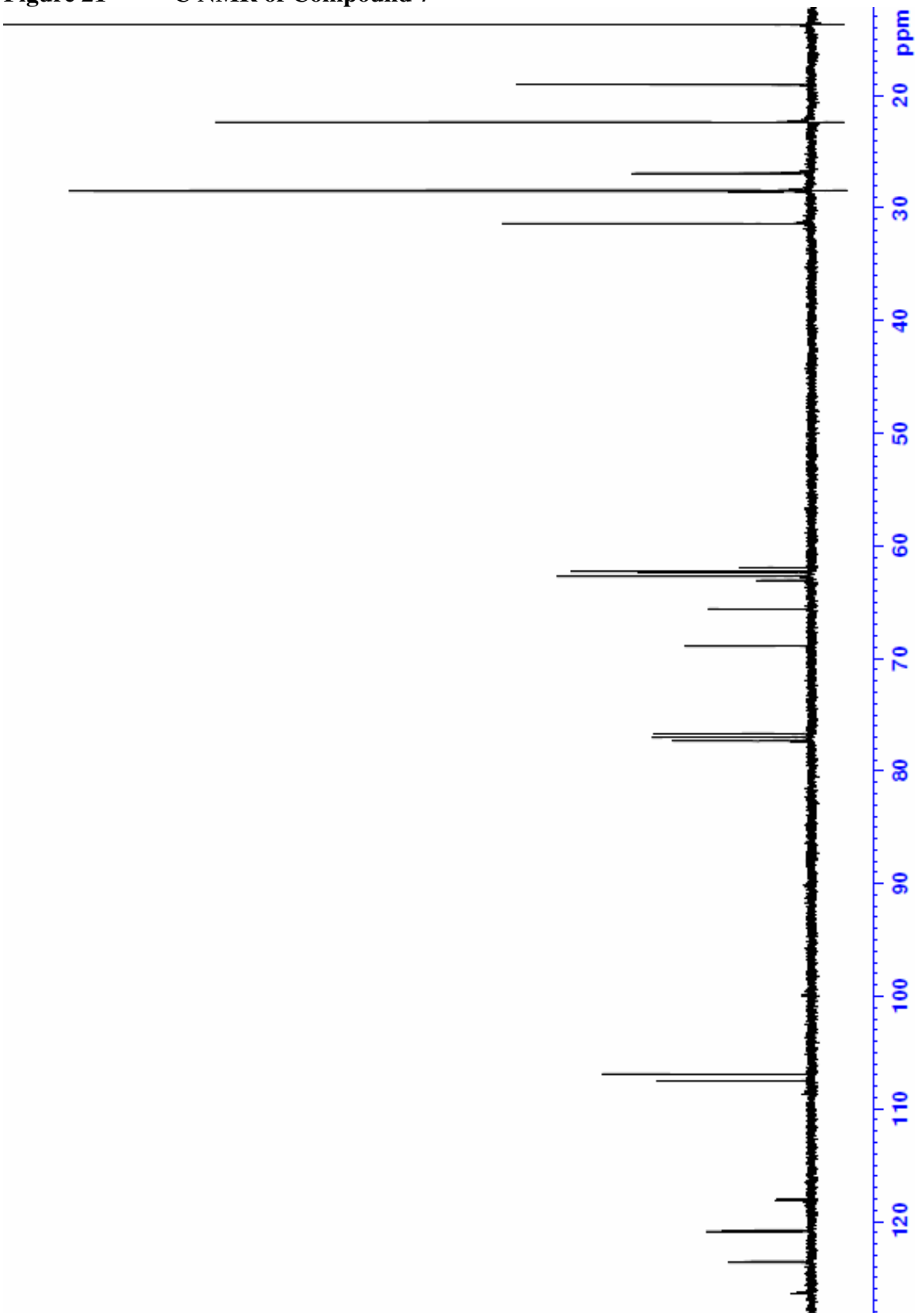


Figure 22 **^{31}P NMR of Compound 7**

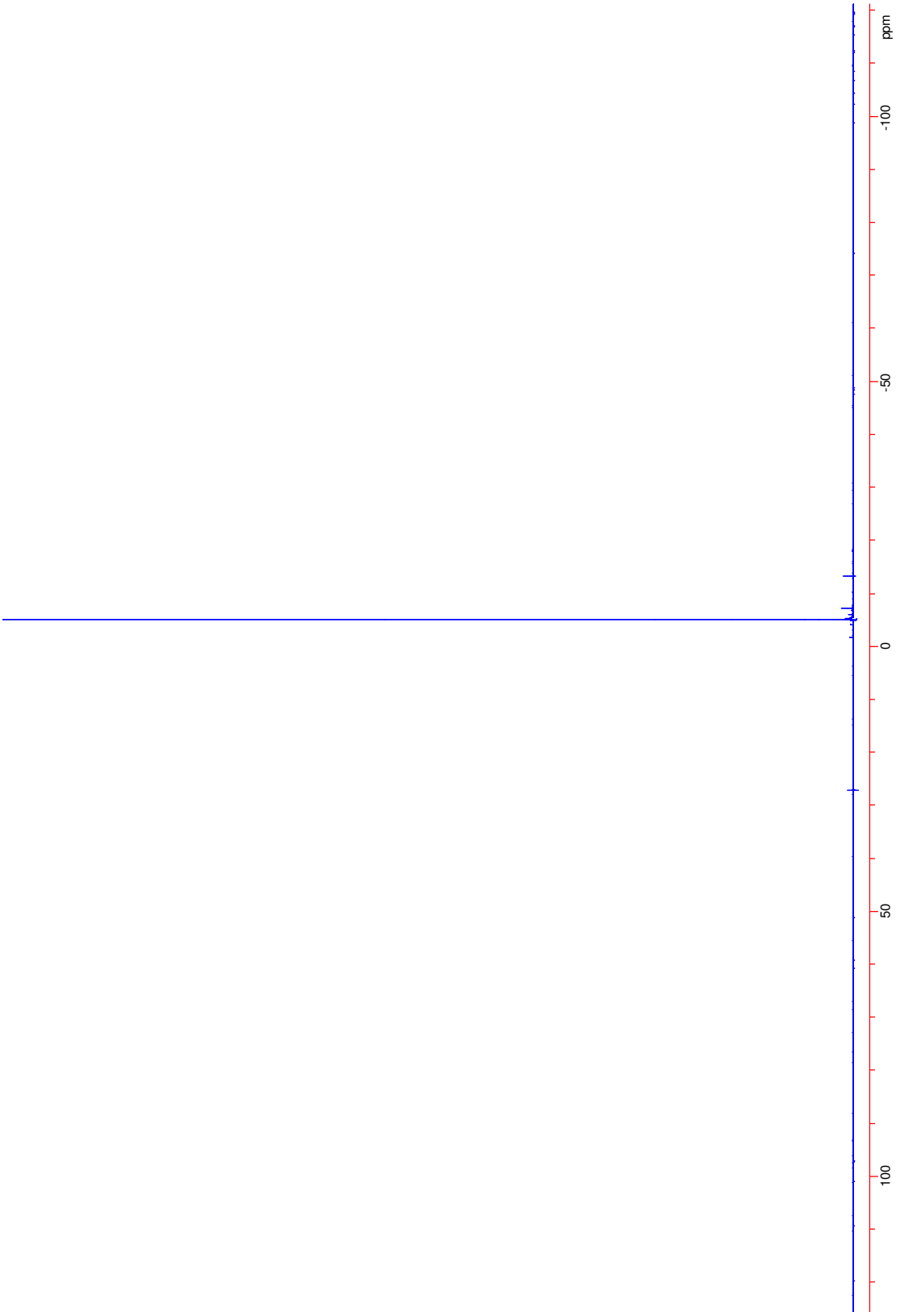


Figure 23 **^{1}H NMR of Compound 8**

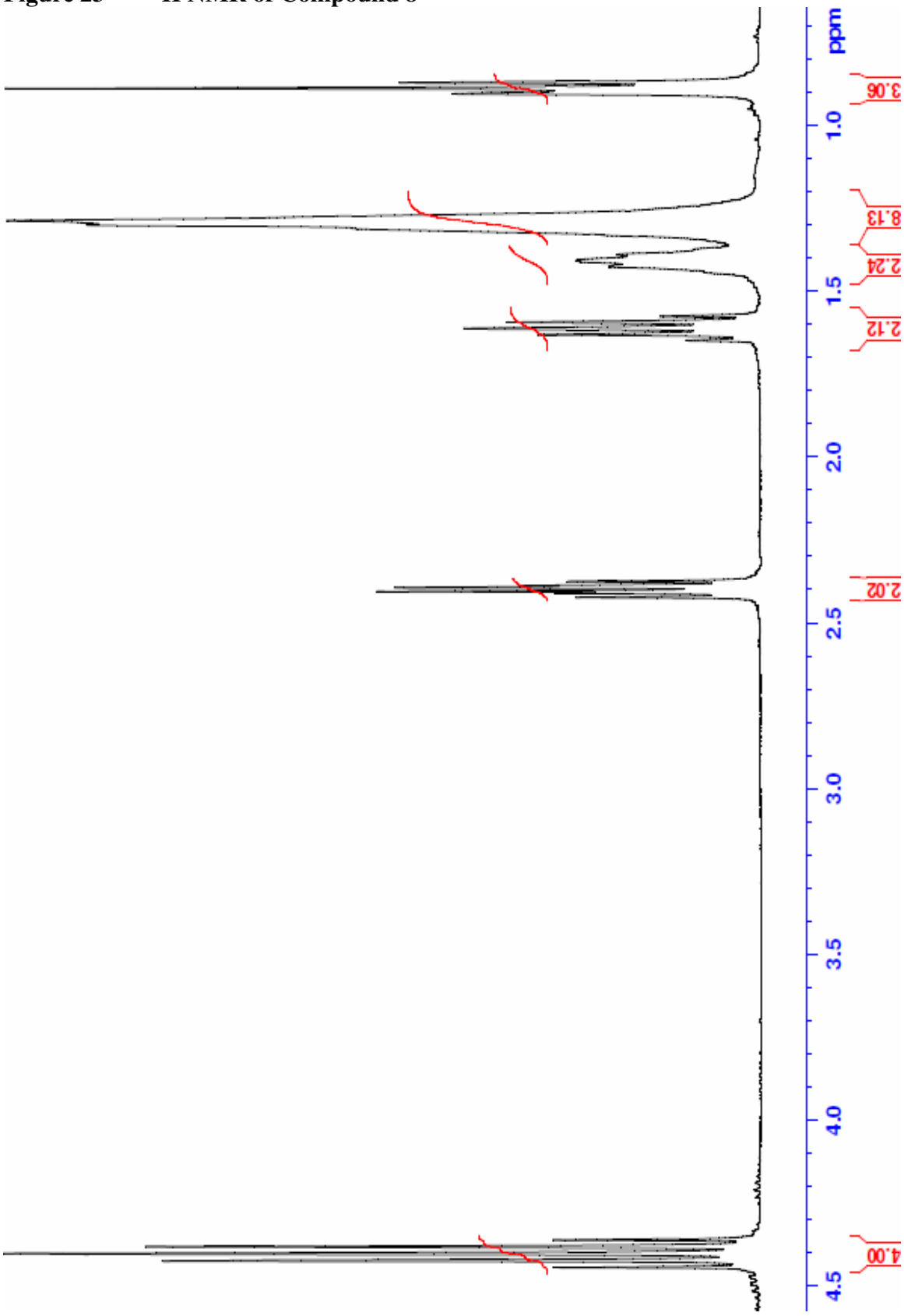


Figure 24 **^{13}C NMR of Compound 8**

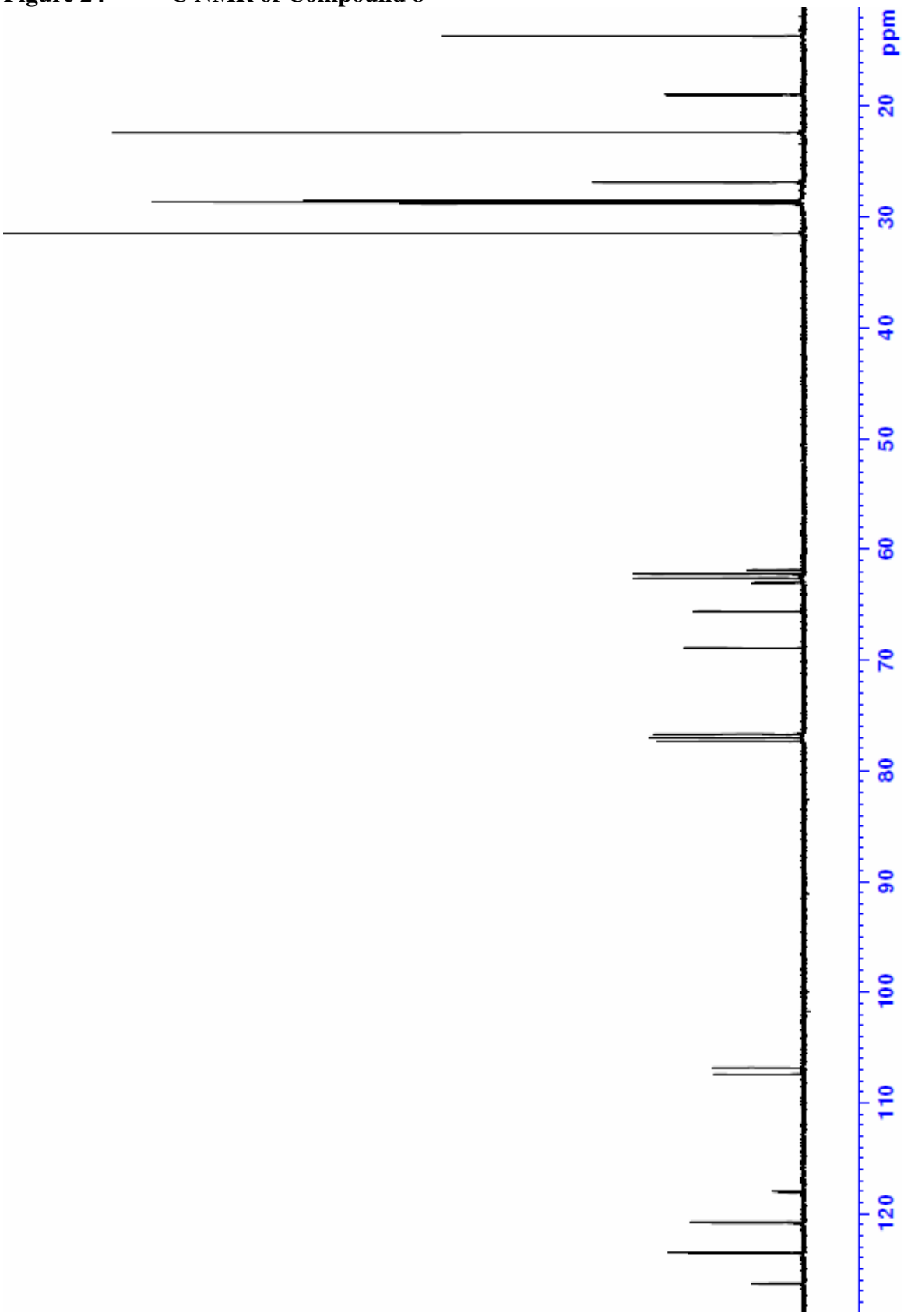


Figure 25 **^{31}P NMR of Compound 8**

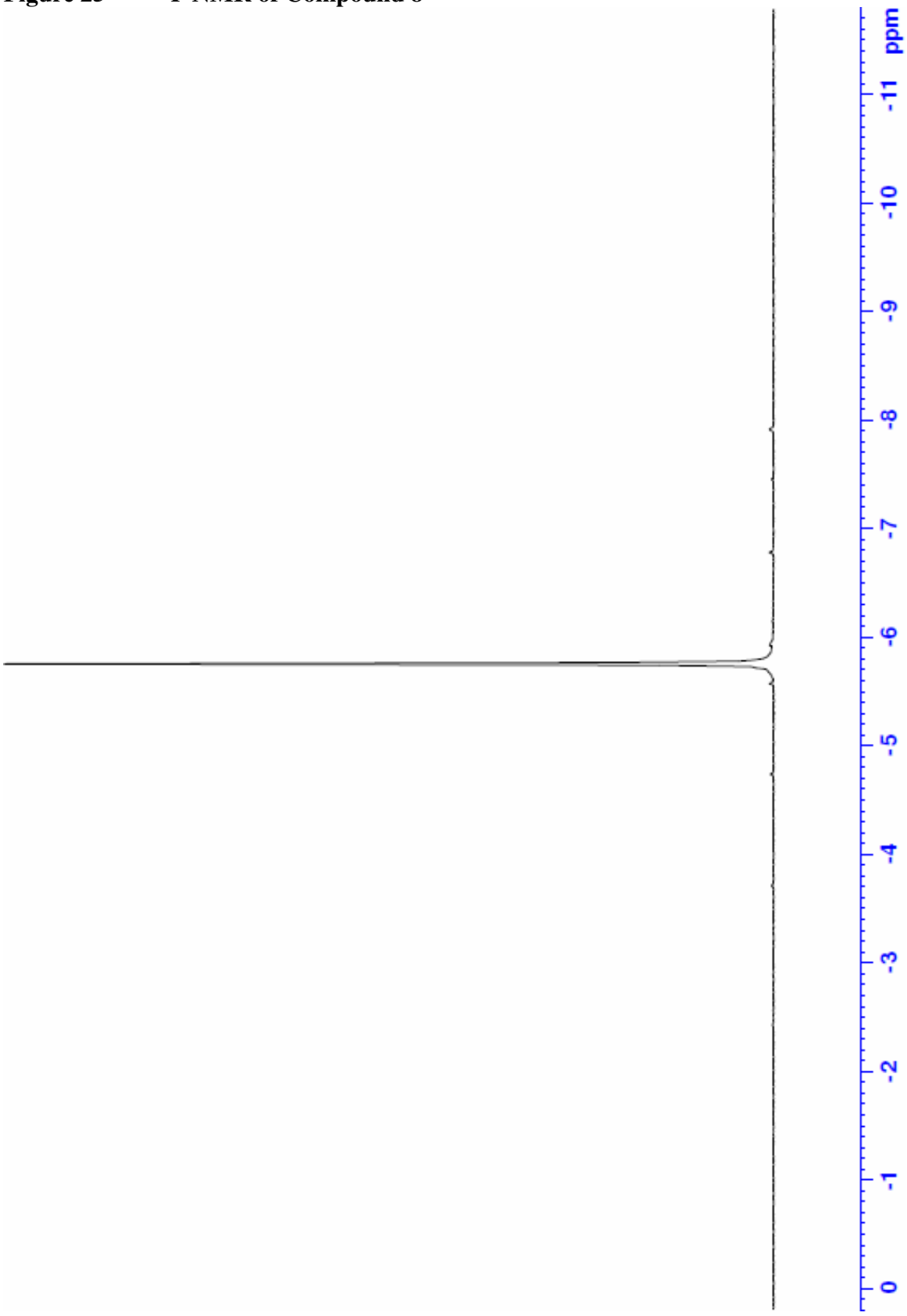


Figure 26 **^{1}H NMR of Compound 10**

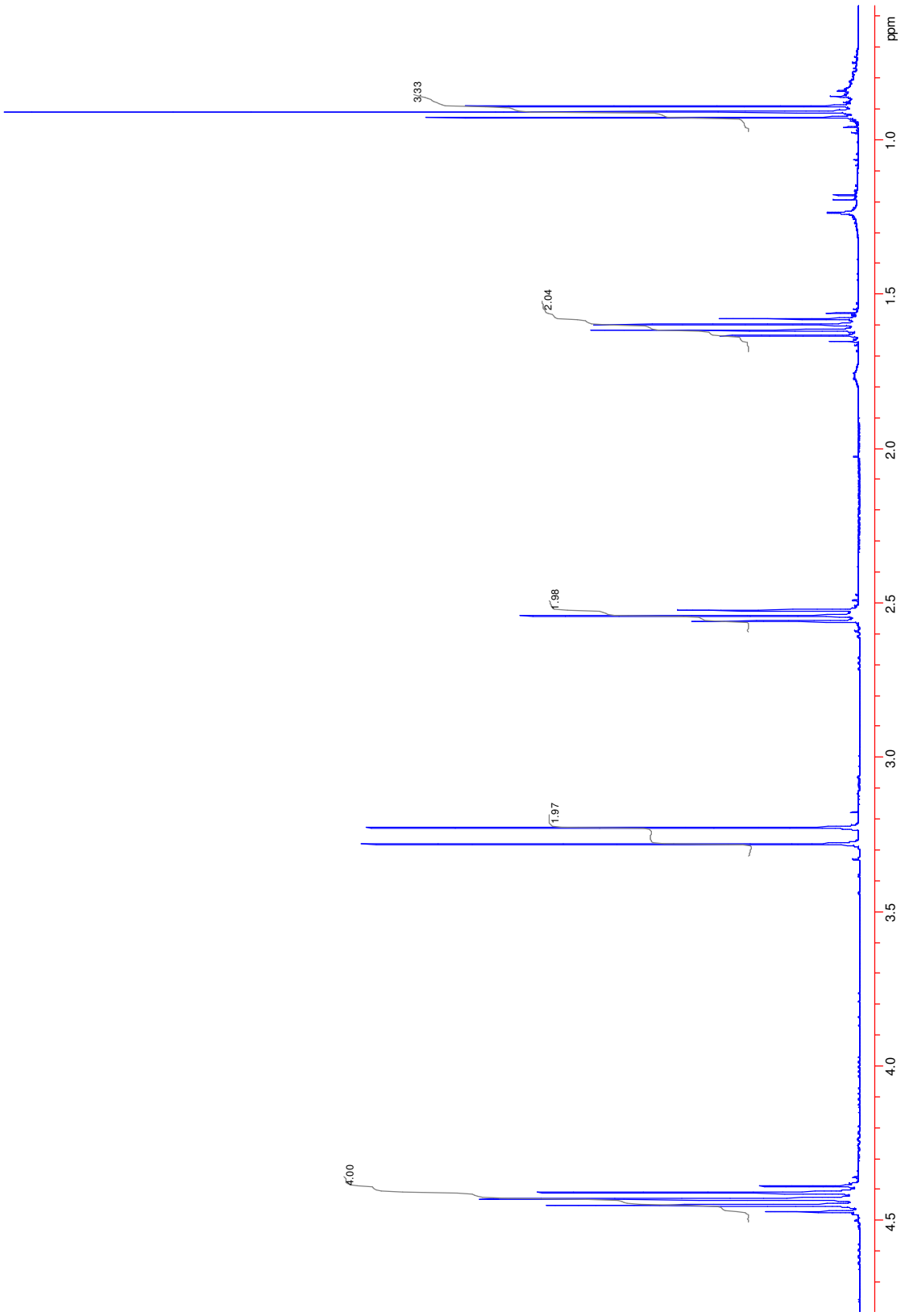


Figure 27 **^{13}C NMR of Compound 10**

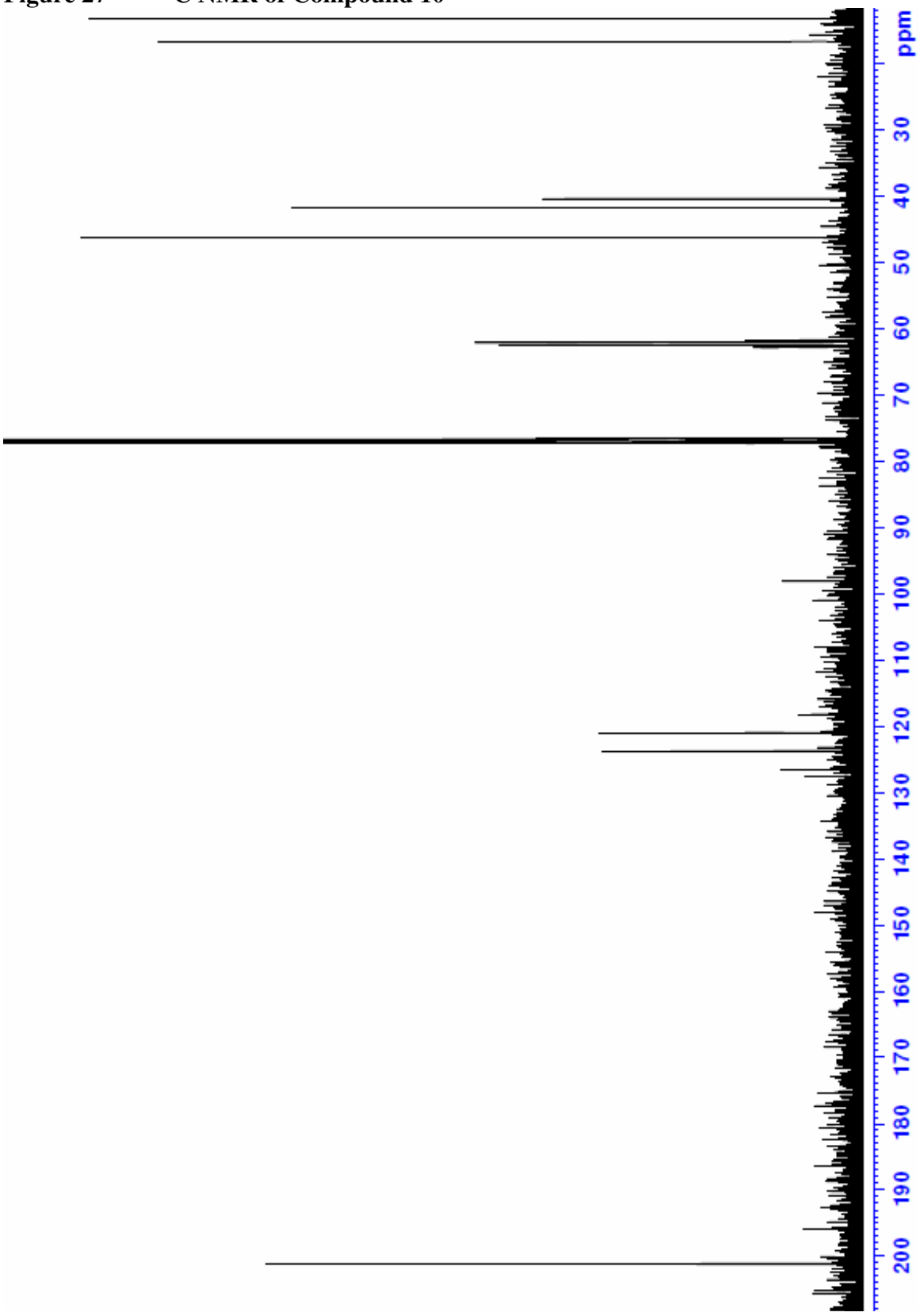


Figure 28 ^{31}P NMR of Compound 10

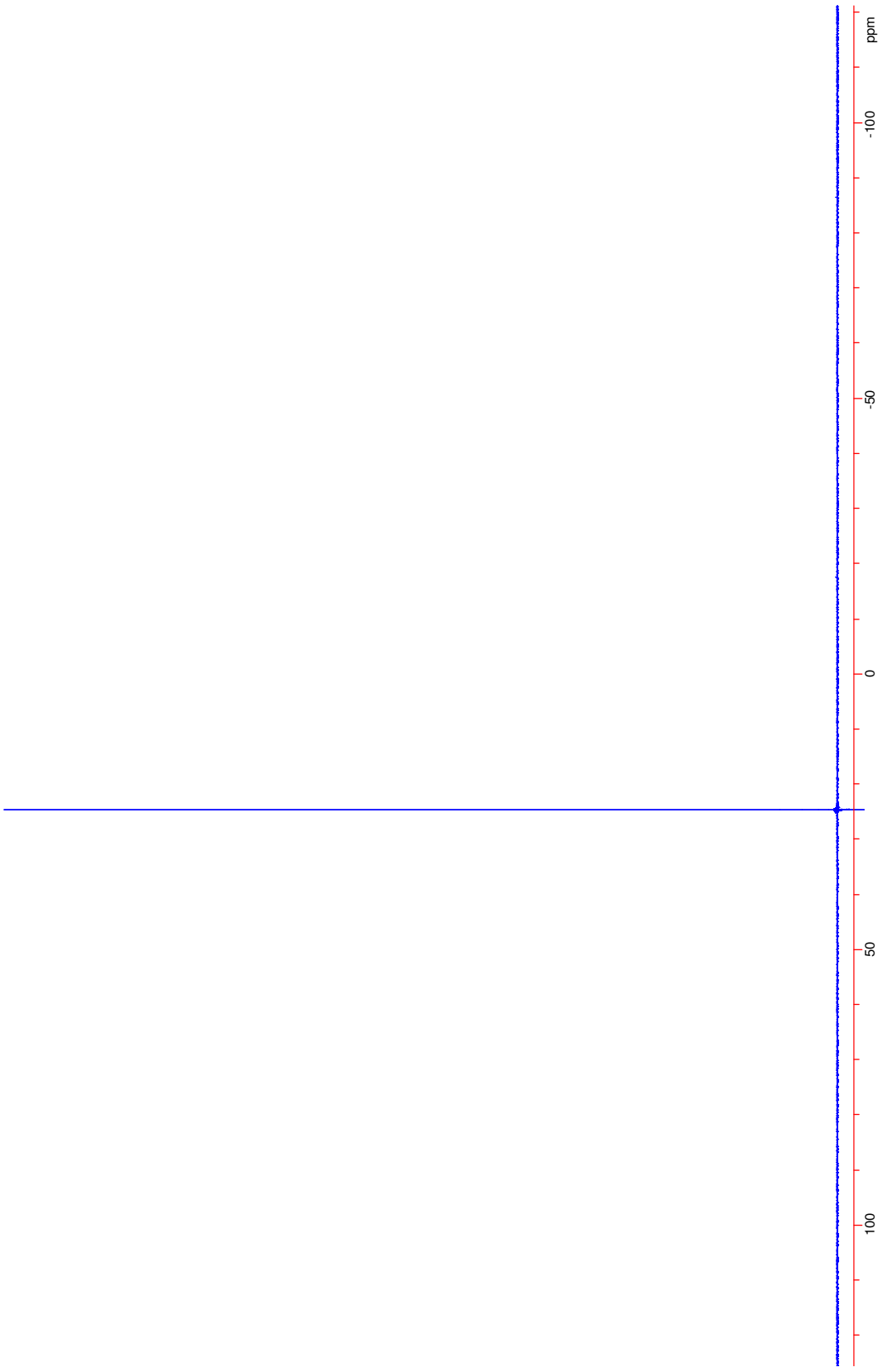


Figure 29 **^{1}H NMR of Compound 11**

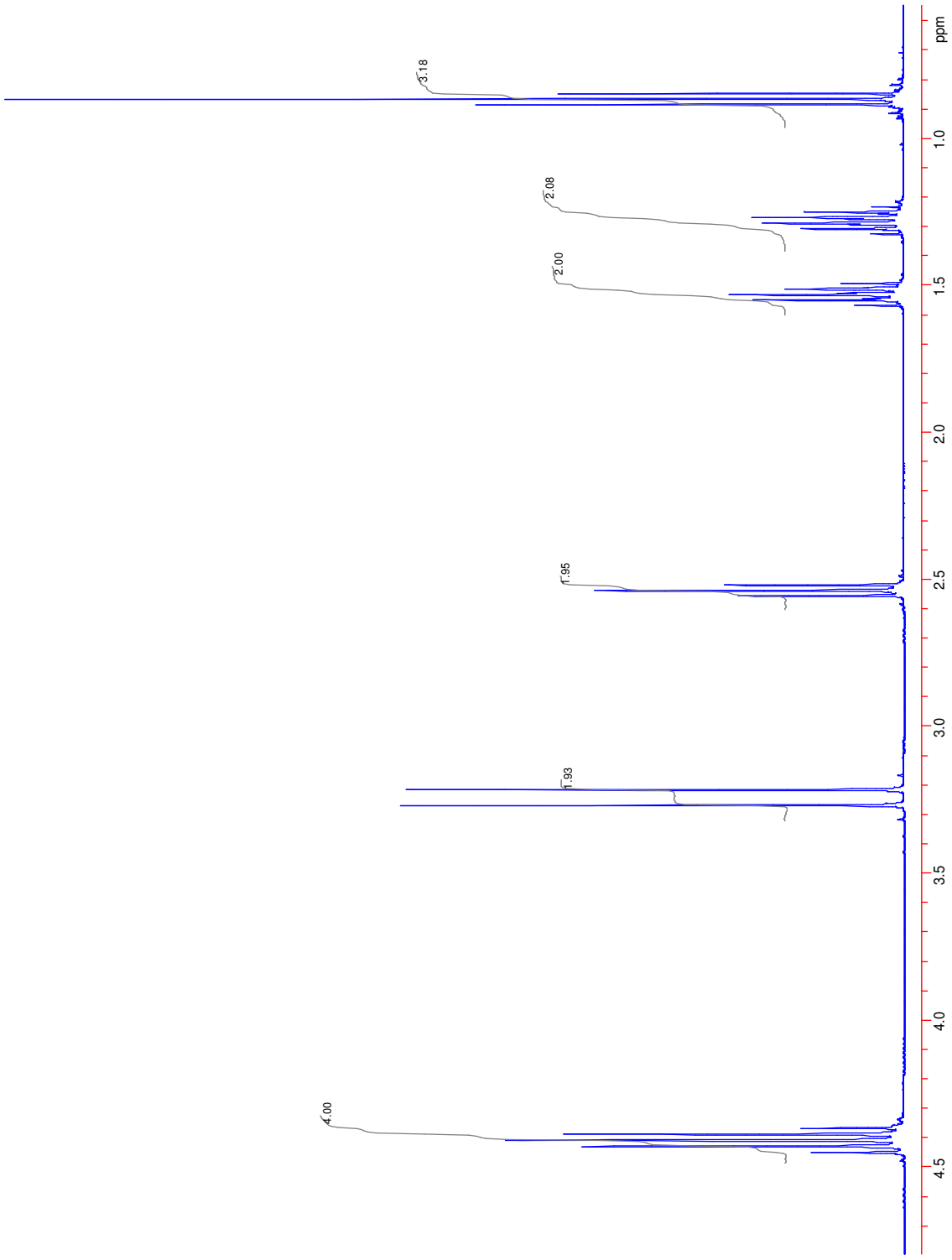


Figure 30 **^{13}C NMR of Compound 11**

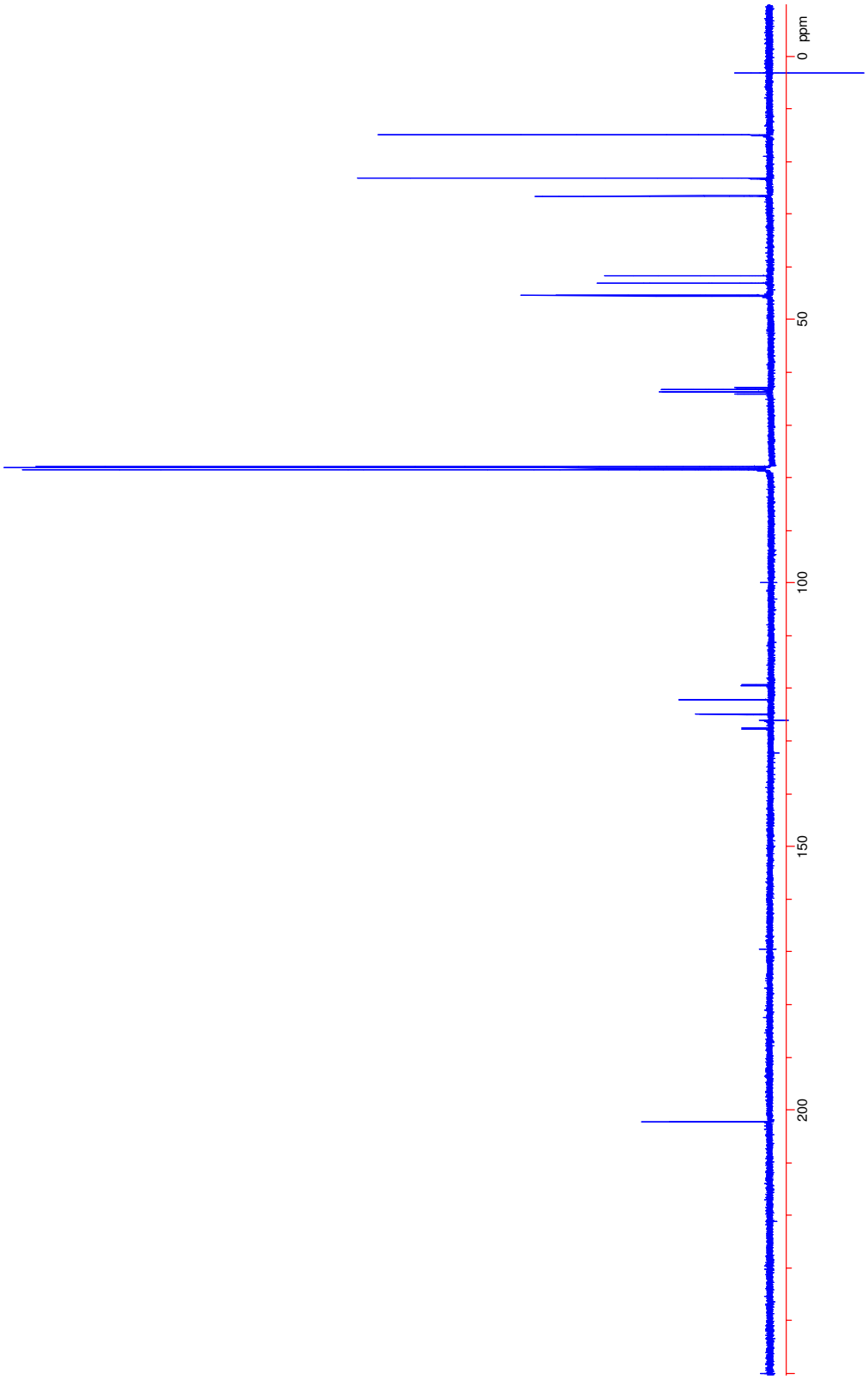


Figure 31 **^{31}P NMR of Compound 11**

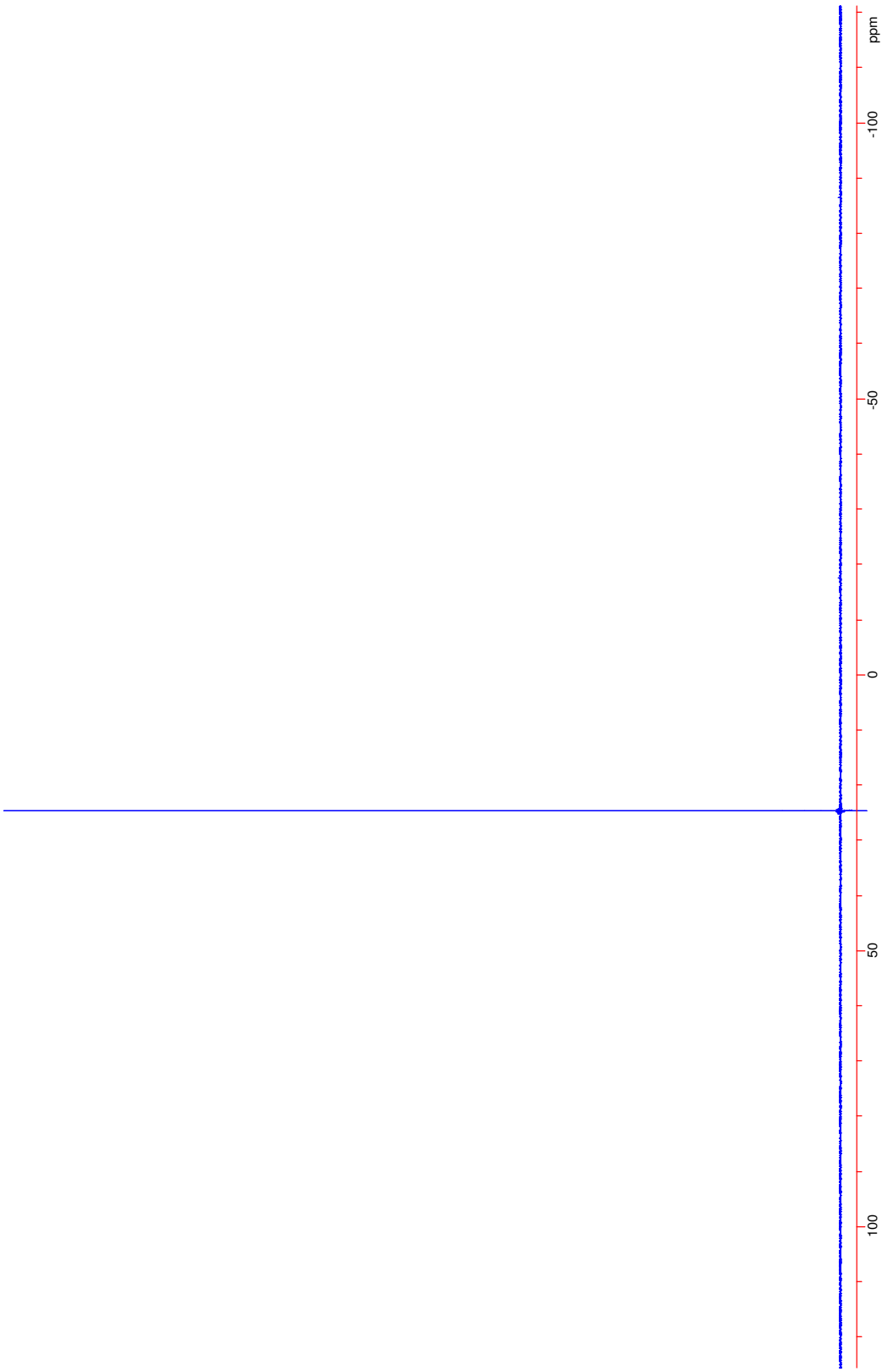


Figure 32 **^{1}H NMR of Compound 12**

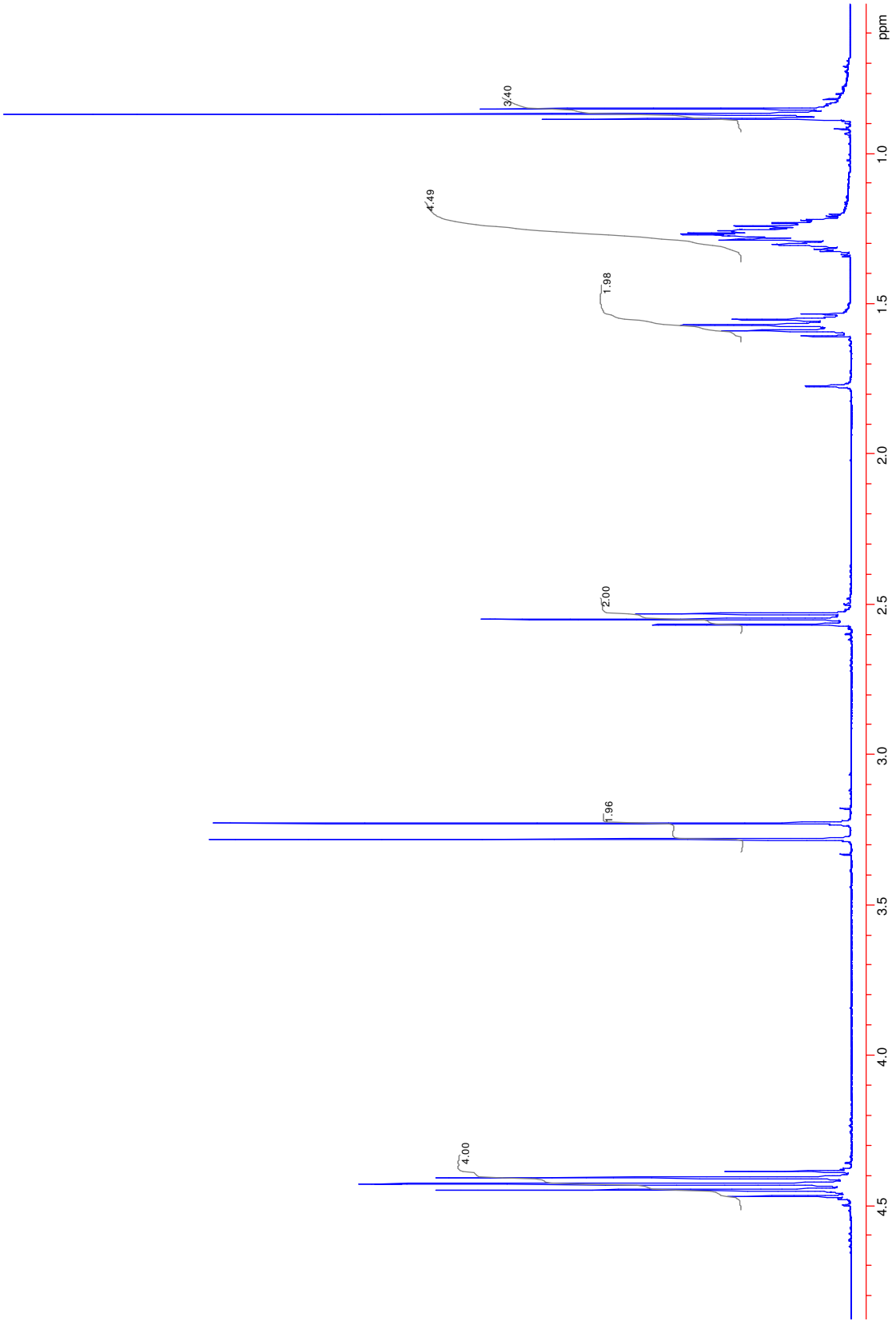


Figure 33 ^{13}C NMR of Compound 12

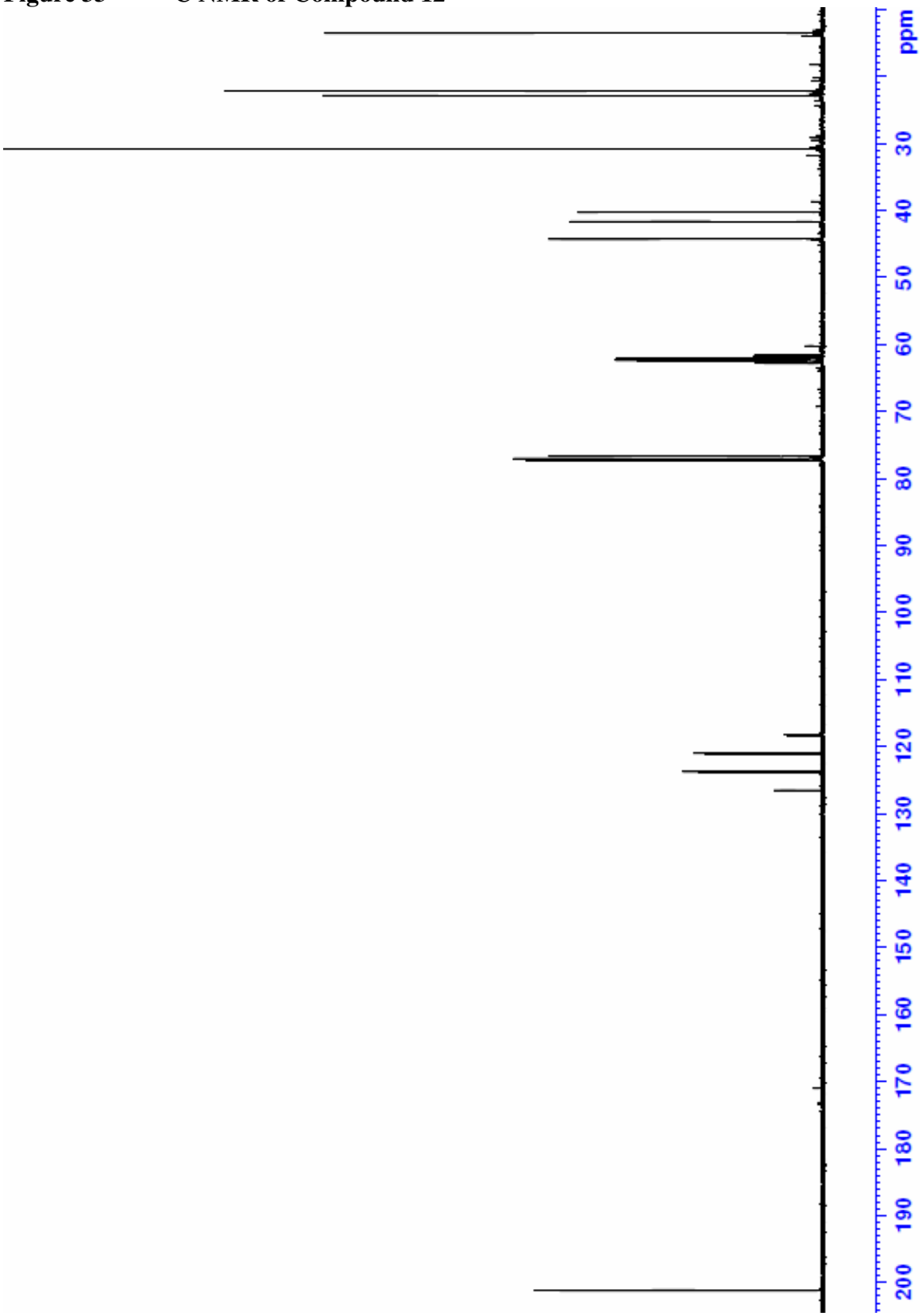


Figure 34 **^{31}P NMR of Compound 12**

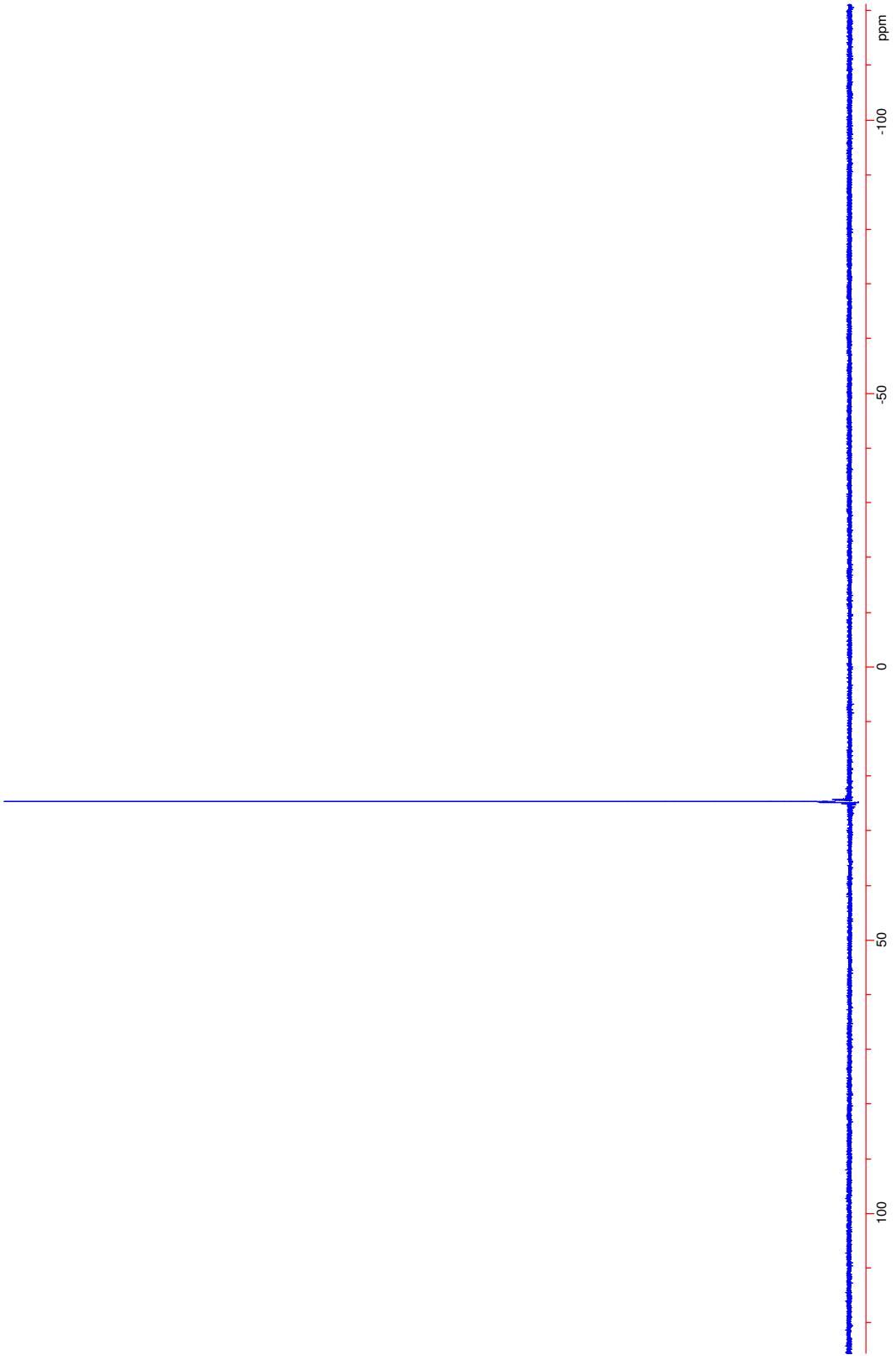


Figure 35 **^{1}H NMR of Compound 13**

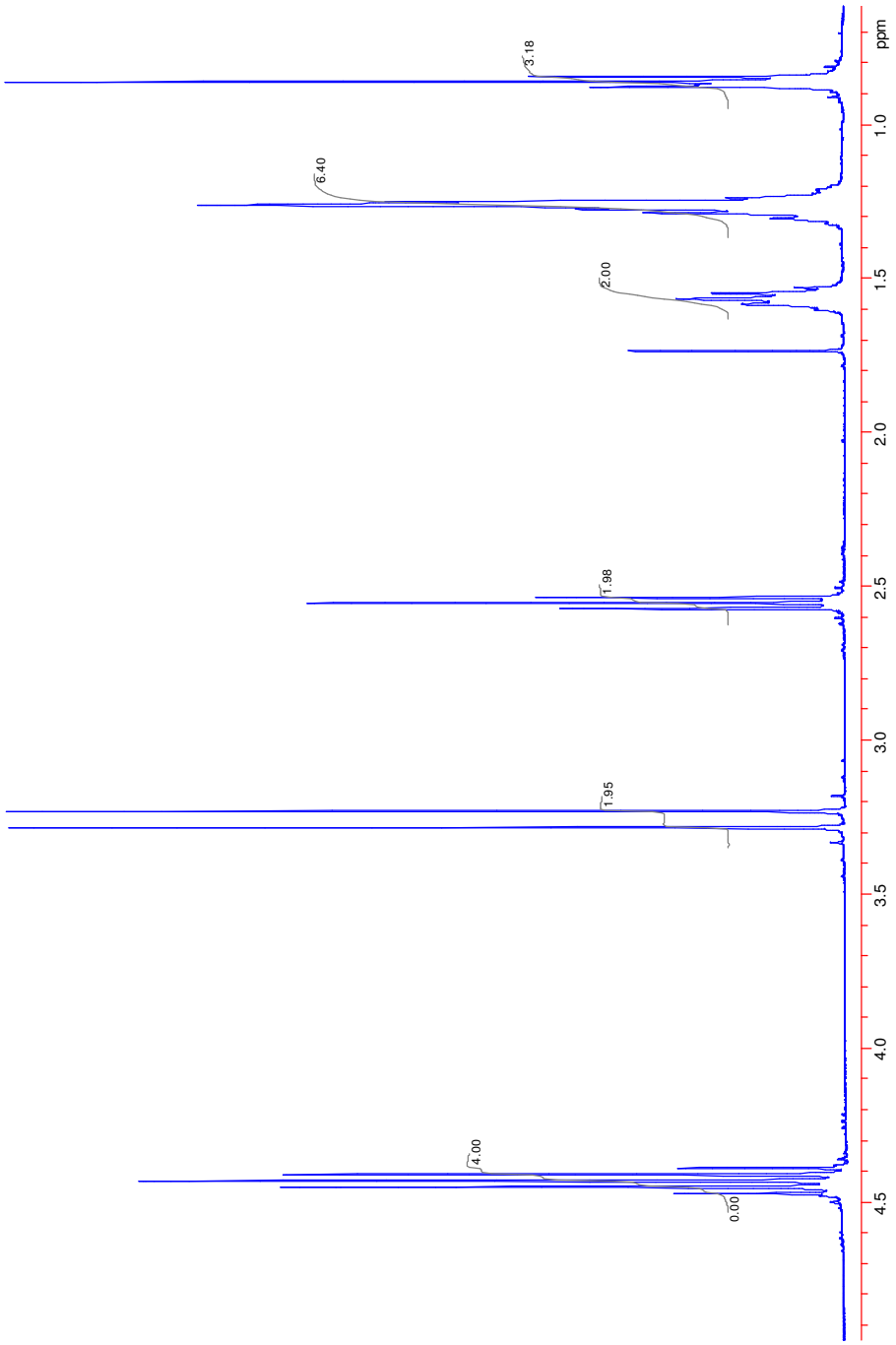


Figure 36 **^{13}C NMR of Compound 13**

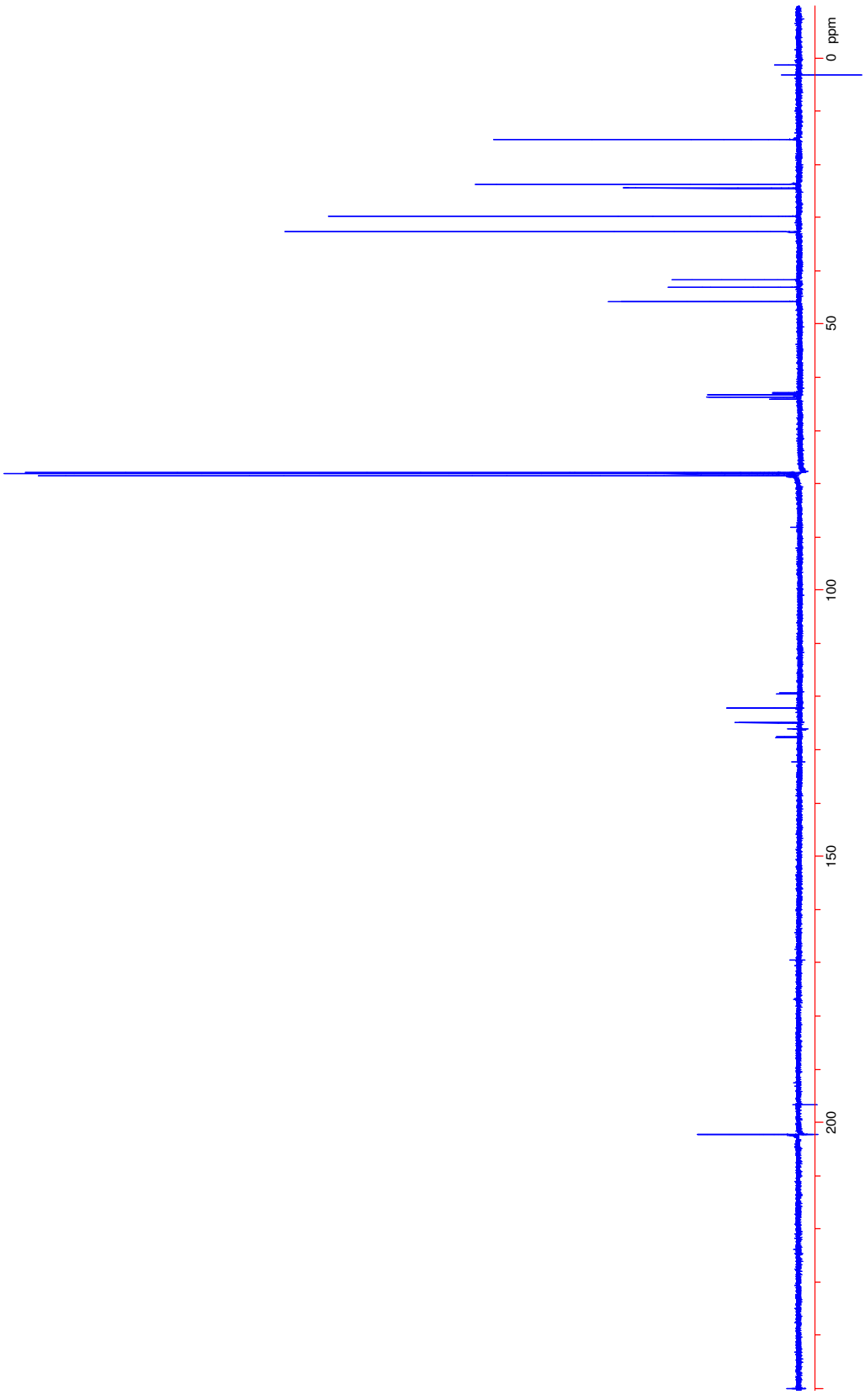


Figure 37 **^{31}P NMR of Compound 13**

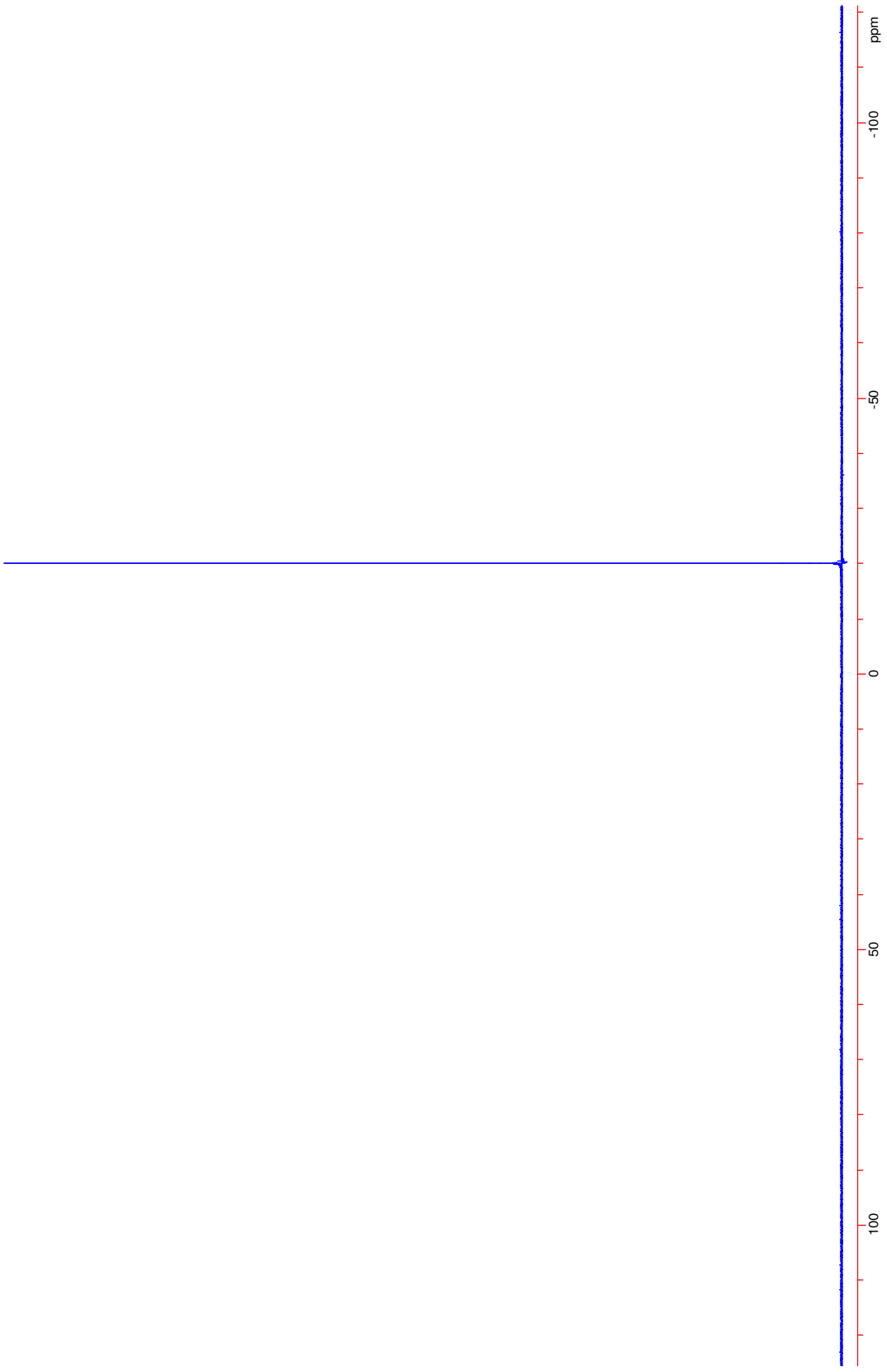


Figure 38 **^{1}H NMR of Compound 14**

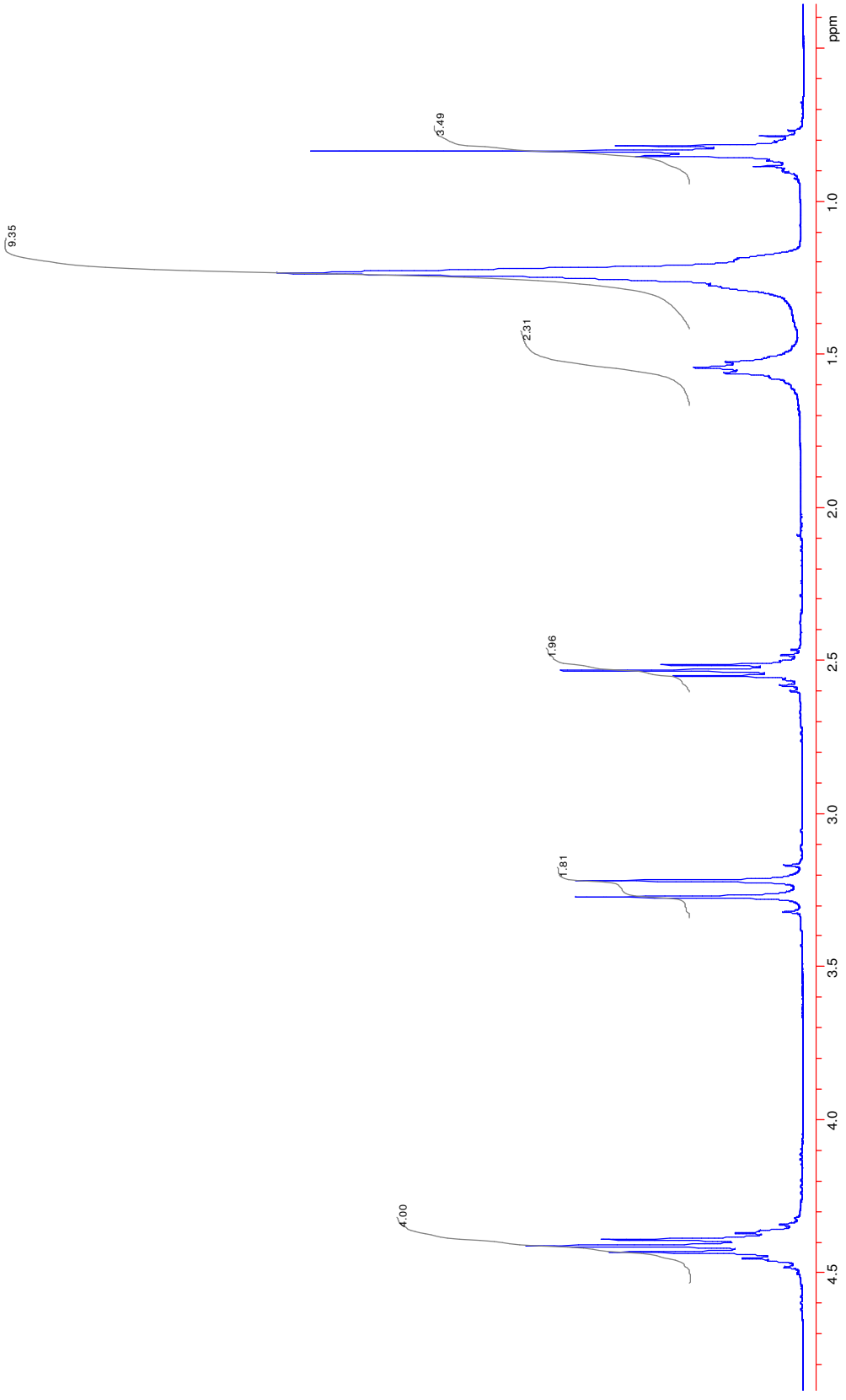


Figure 39 ^{13}C NMR of Compound 14

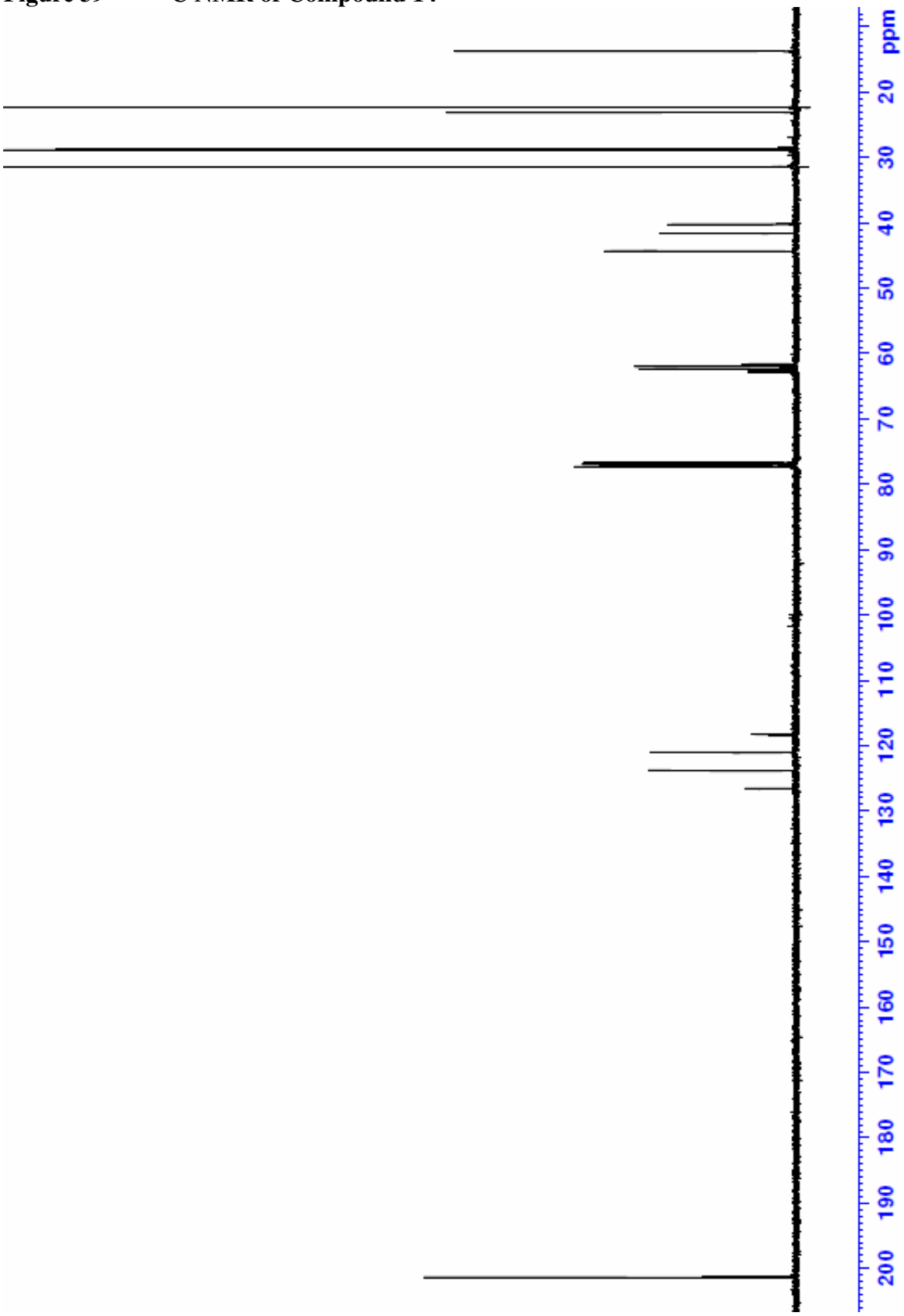


Figure 40 **^{31}P NMR of Compound 14**

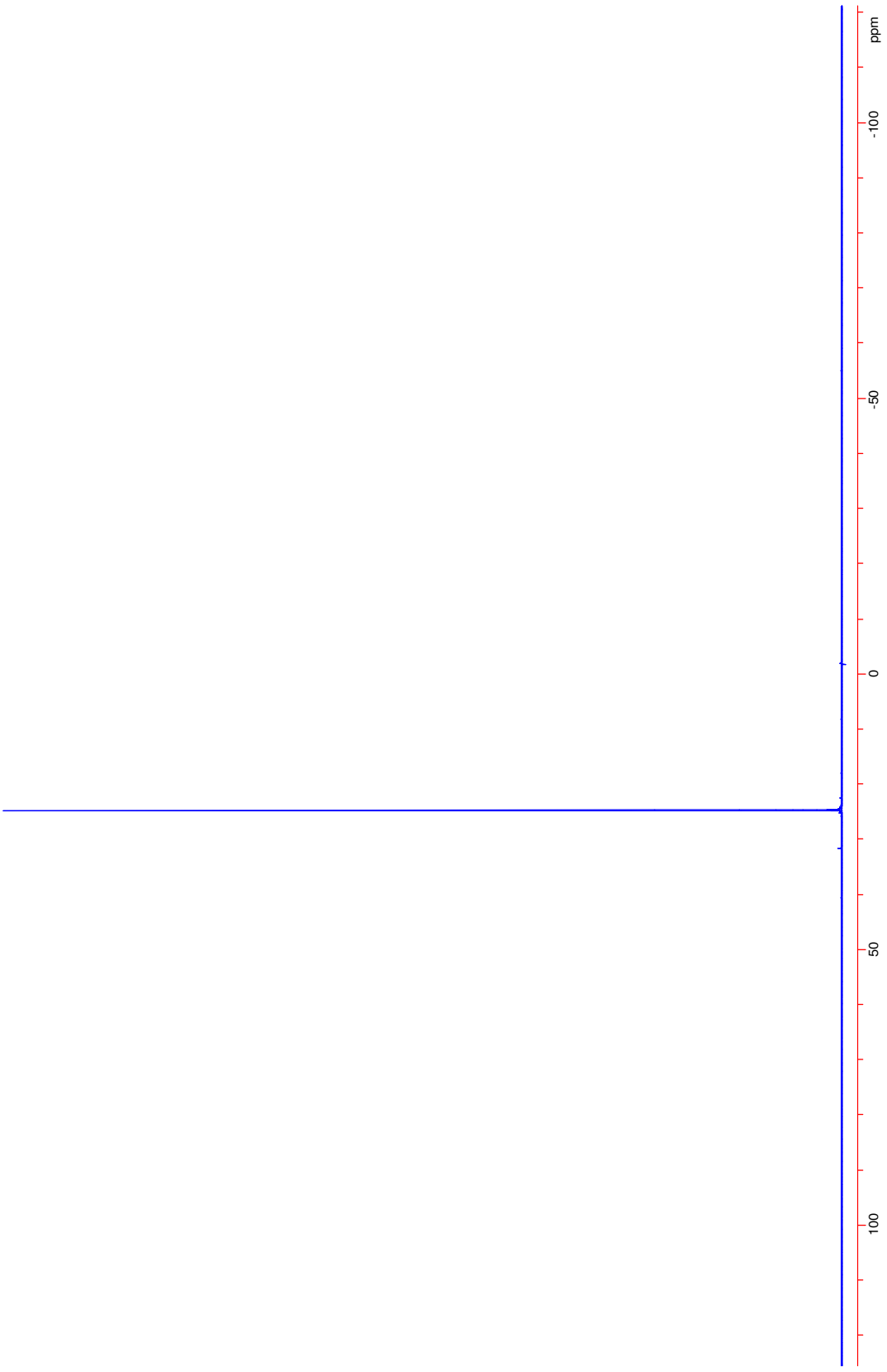


Figure 41 **^{1}H NMR of Compound 15**

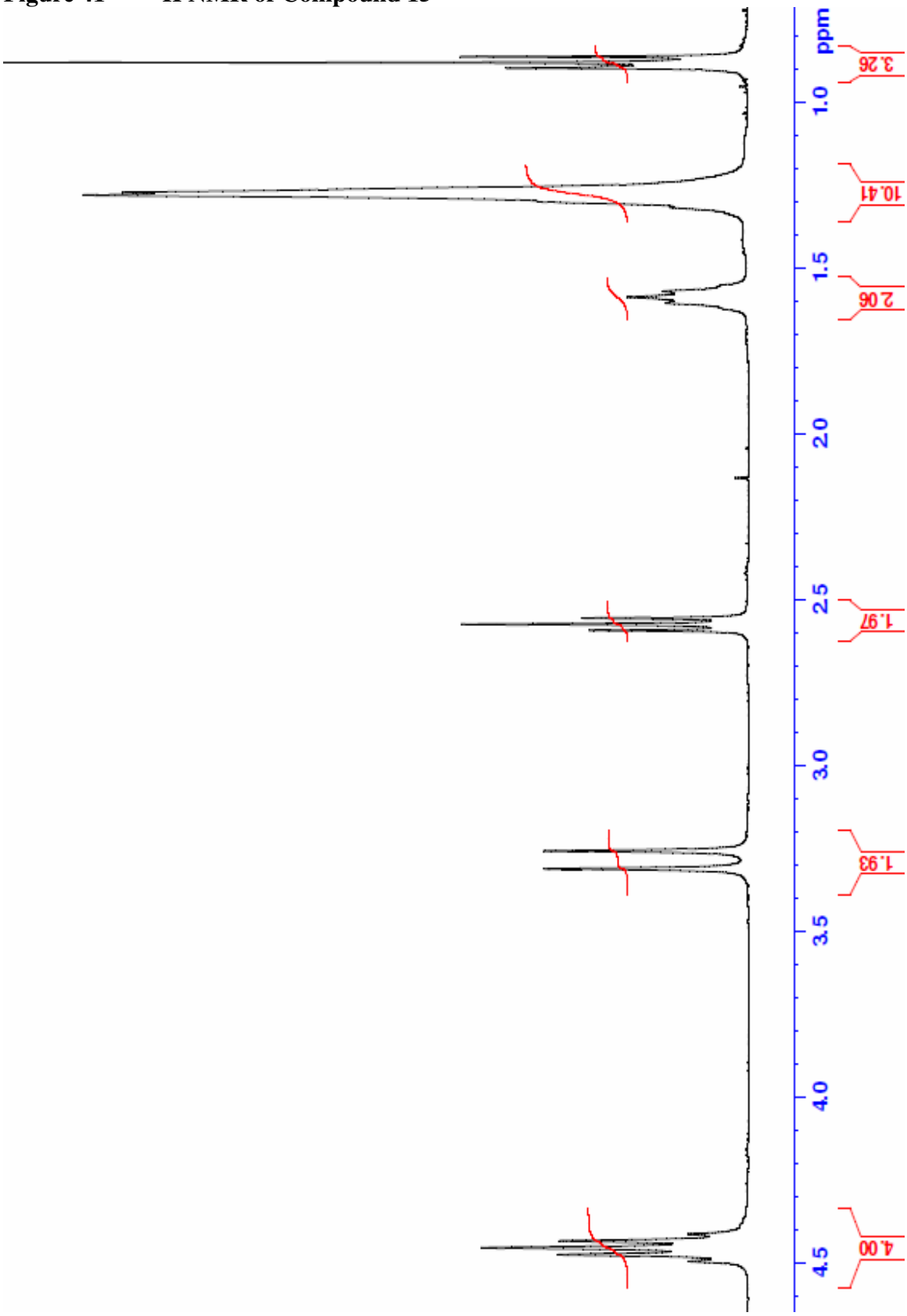


Figure 42 **^{13}C NMR of Compound 15**

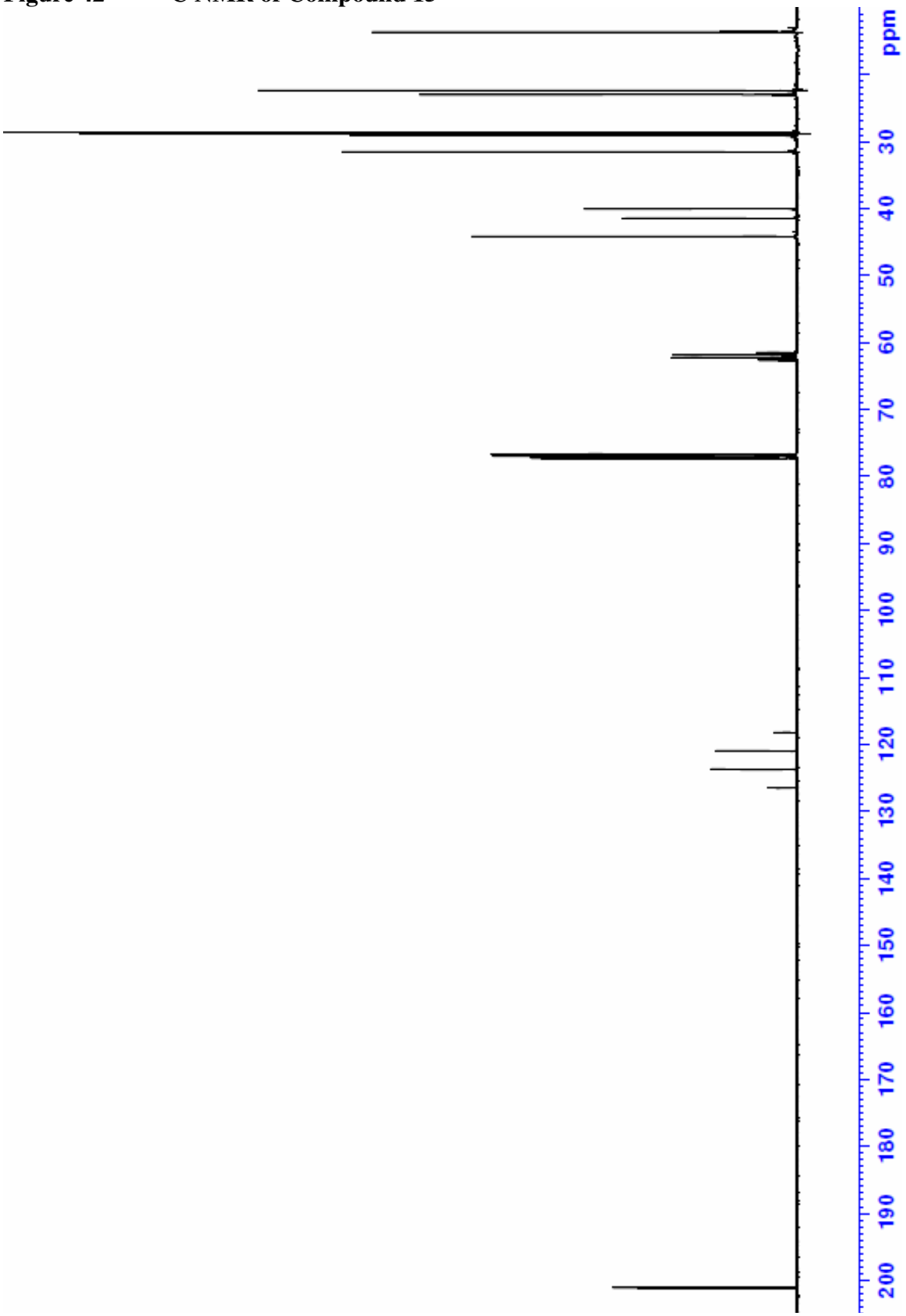


Figure 43 **^{31}P NMR of Compound 15**

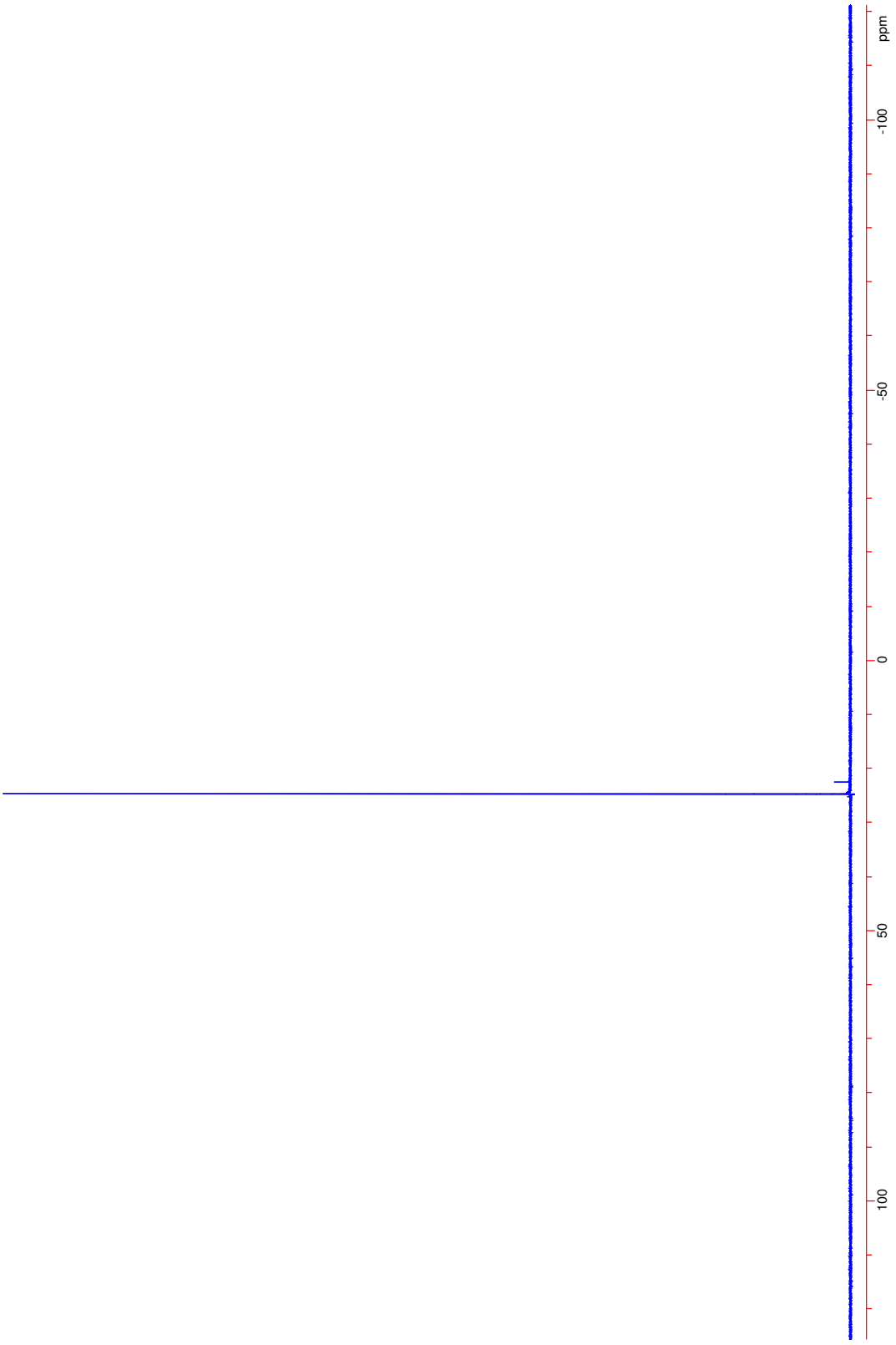


Figure 44 ^{1}H NMR of Compound 16

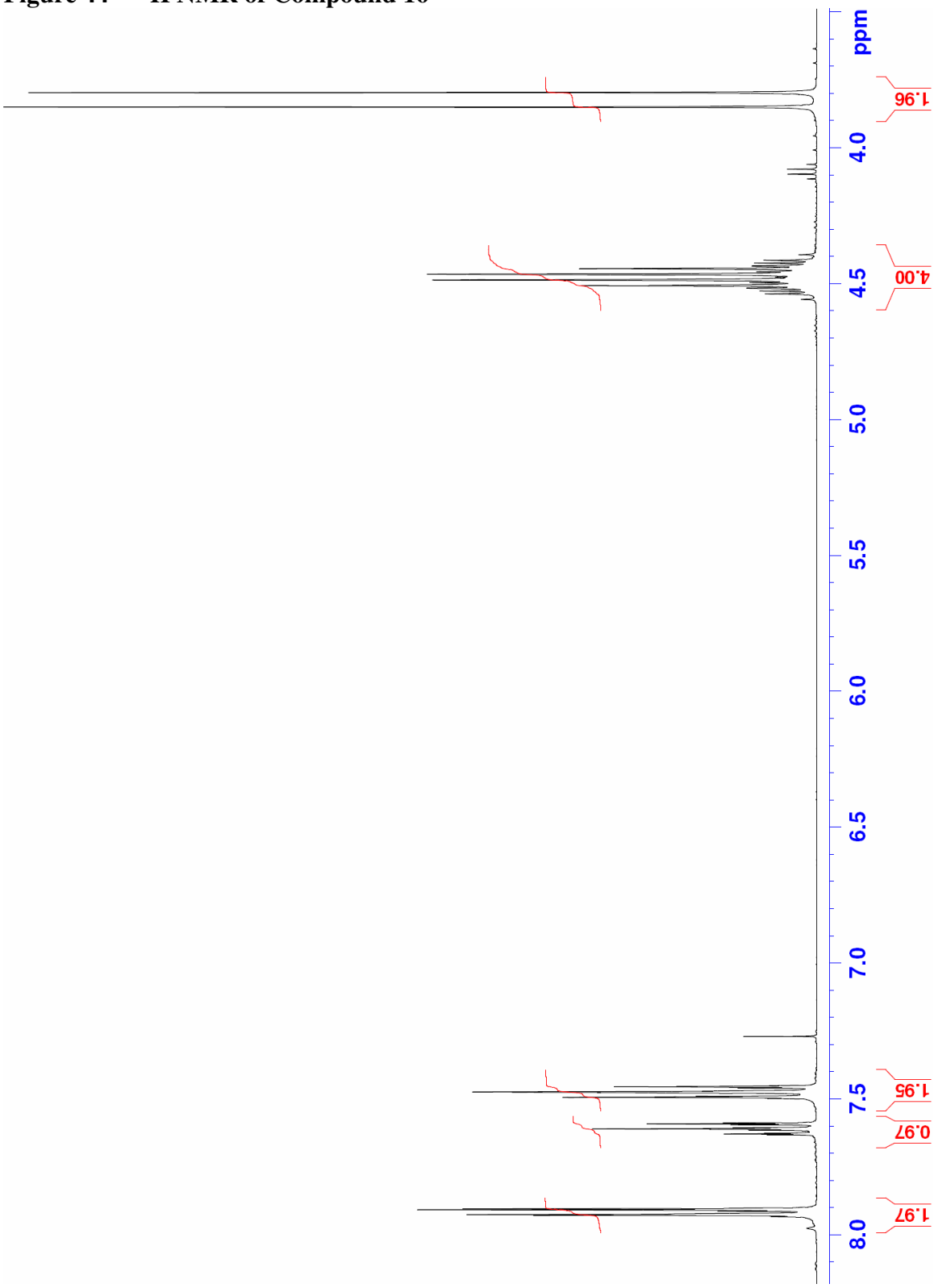


Figure 45 ^{13}C NMR of Compound 16

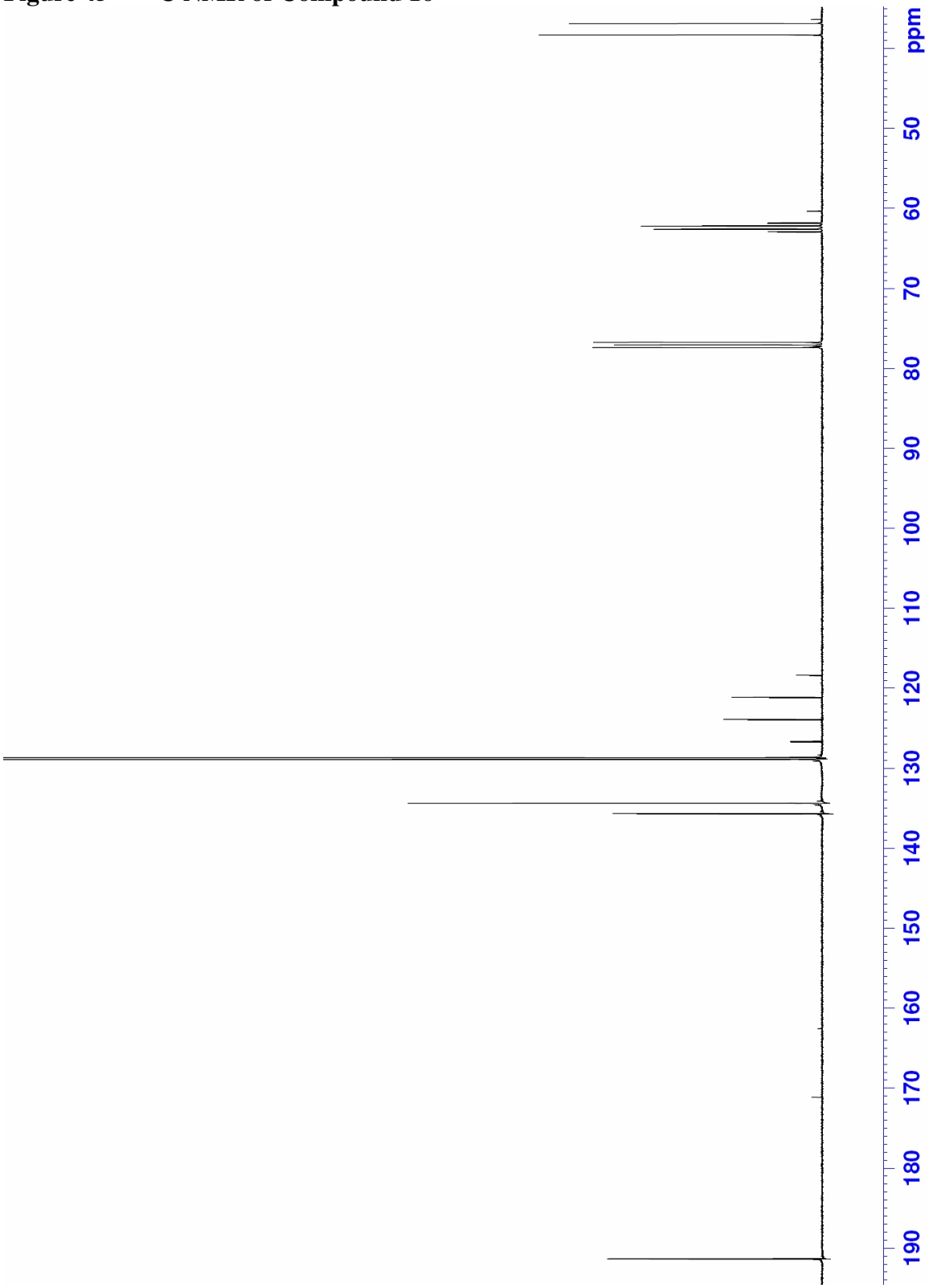


Figure 46 ^{31}P NMR of Compound 16

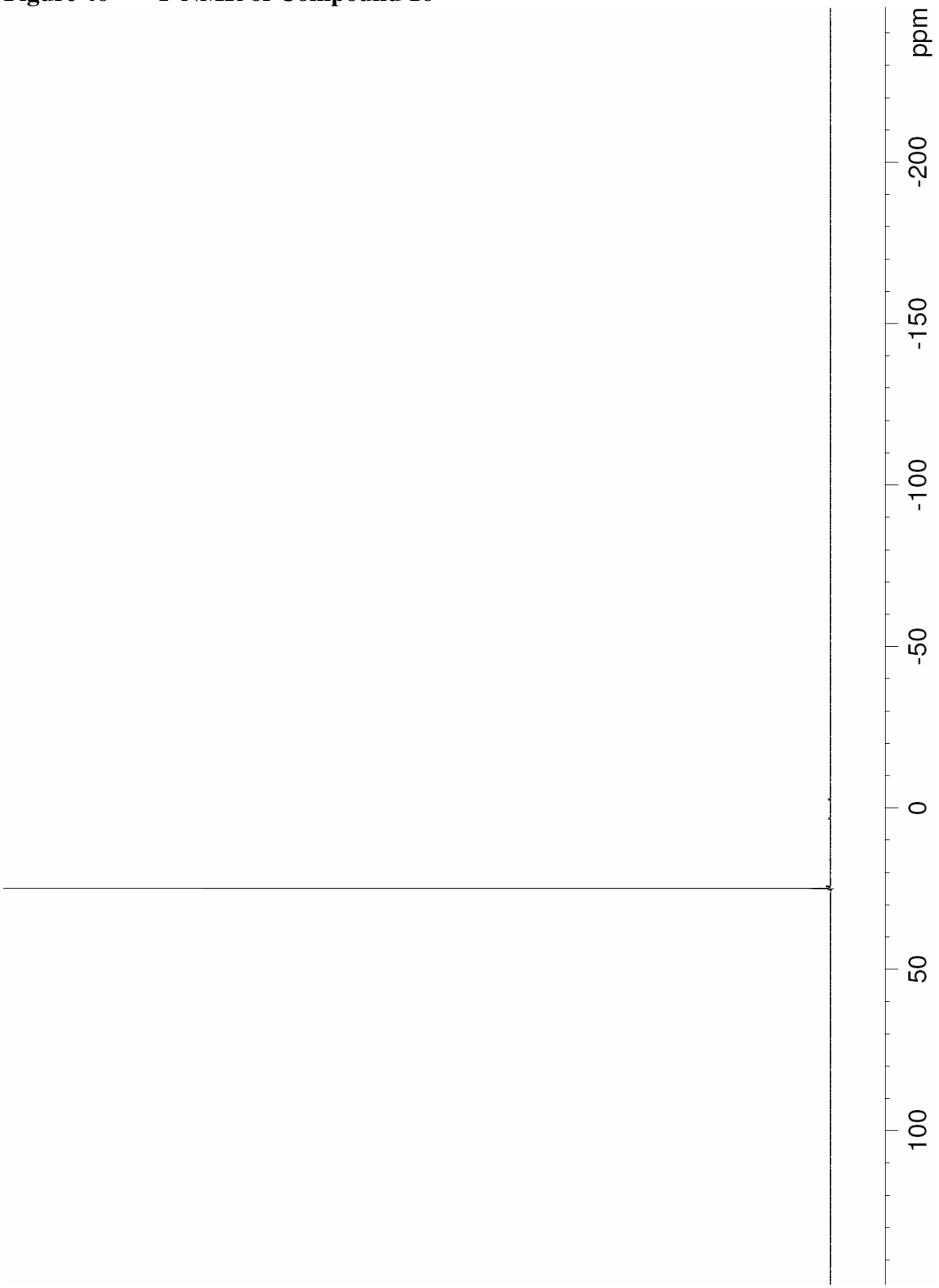


Figure 47 **^{1}H NMR of Compound 17**

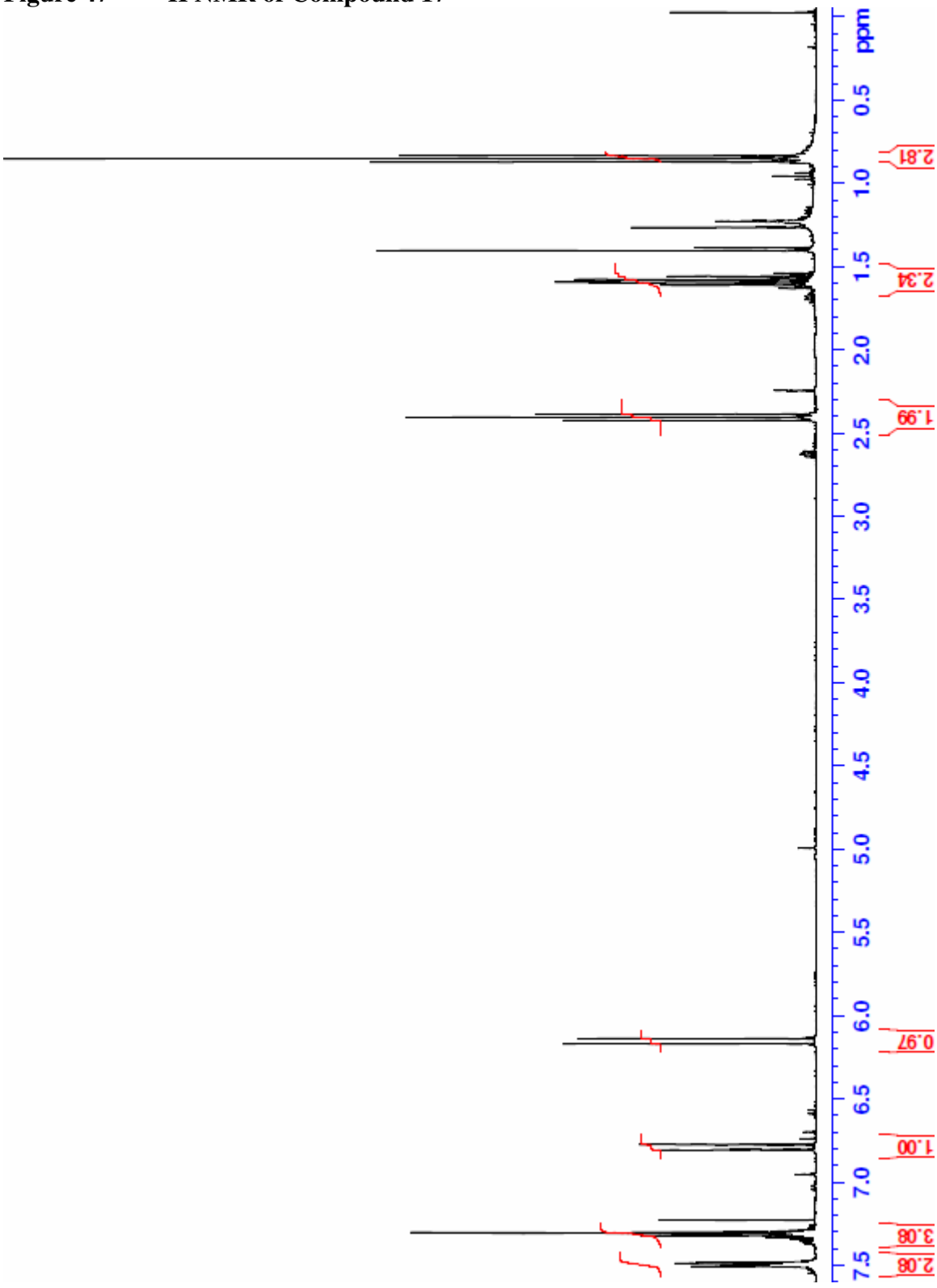


Figure 48 ^{13}C NMR of Compound 17

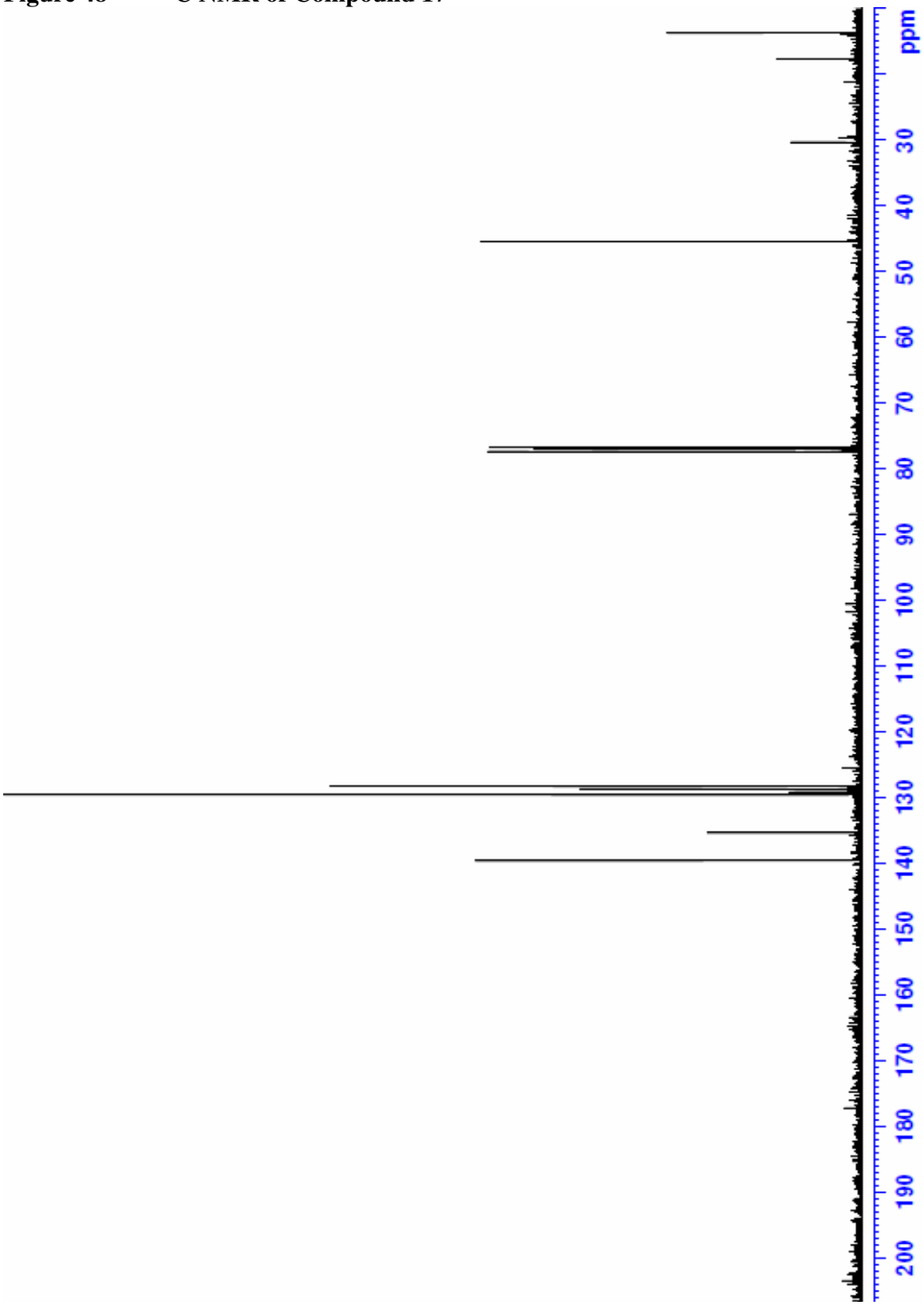


Figure 49 **^{1}H NMR of Compound 18**

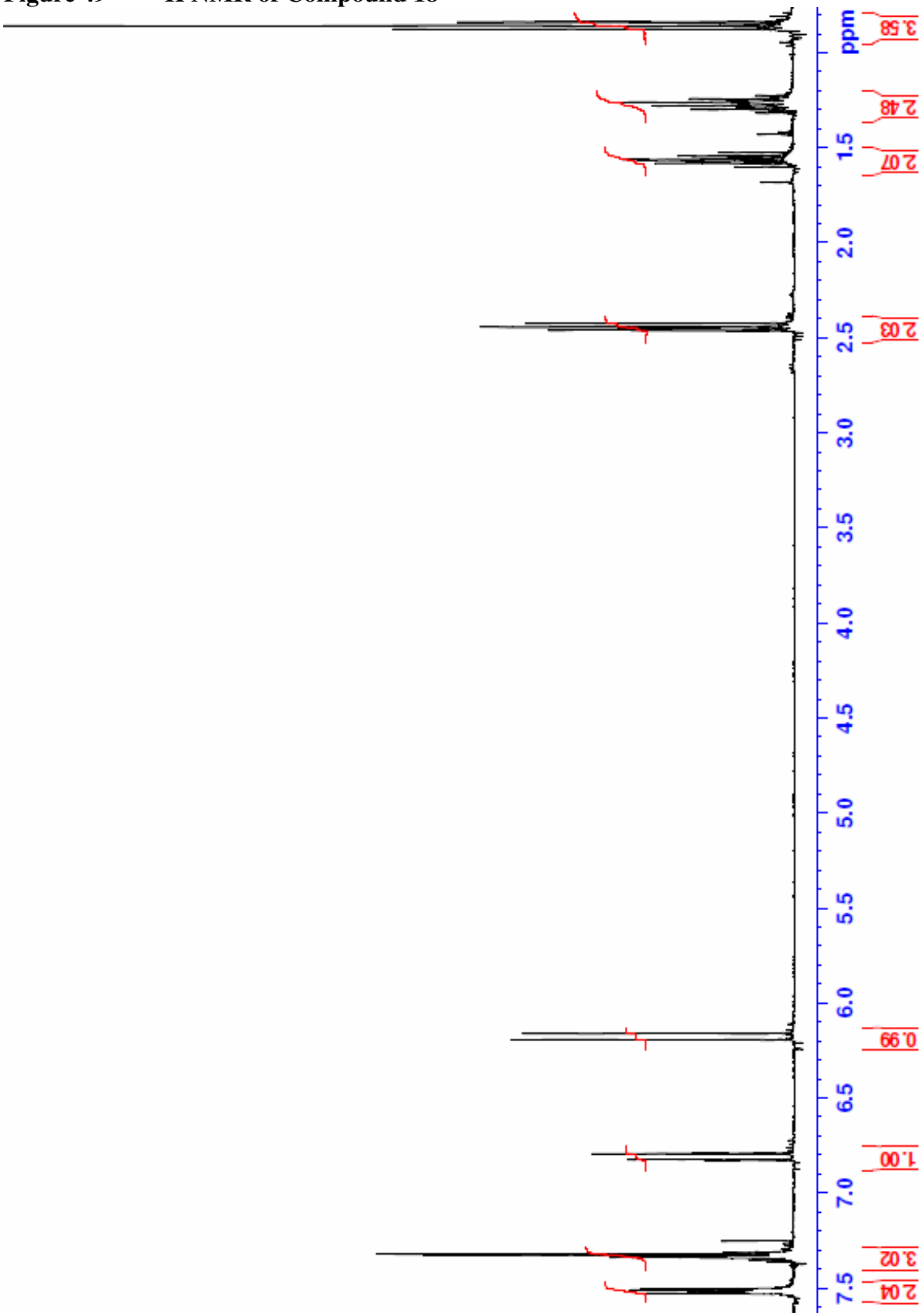


Figure 50 ^{13}C NMR of Compound 18

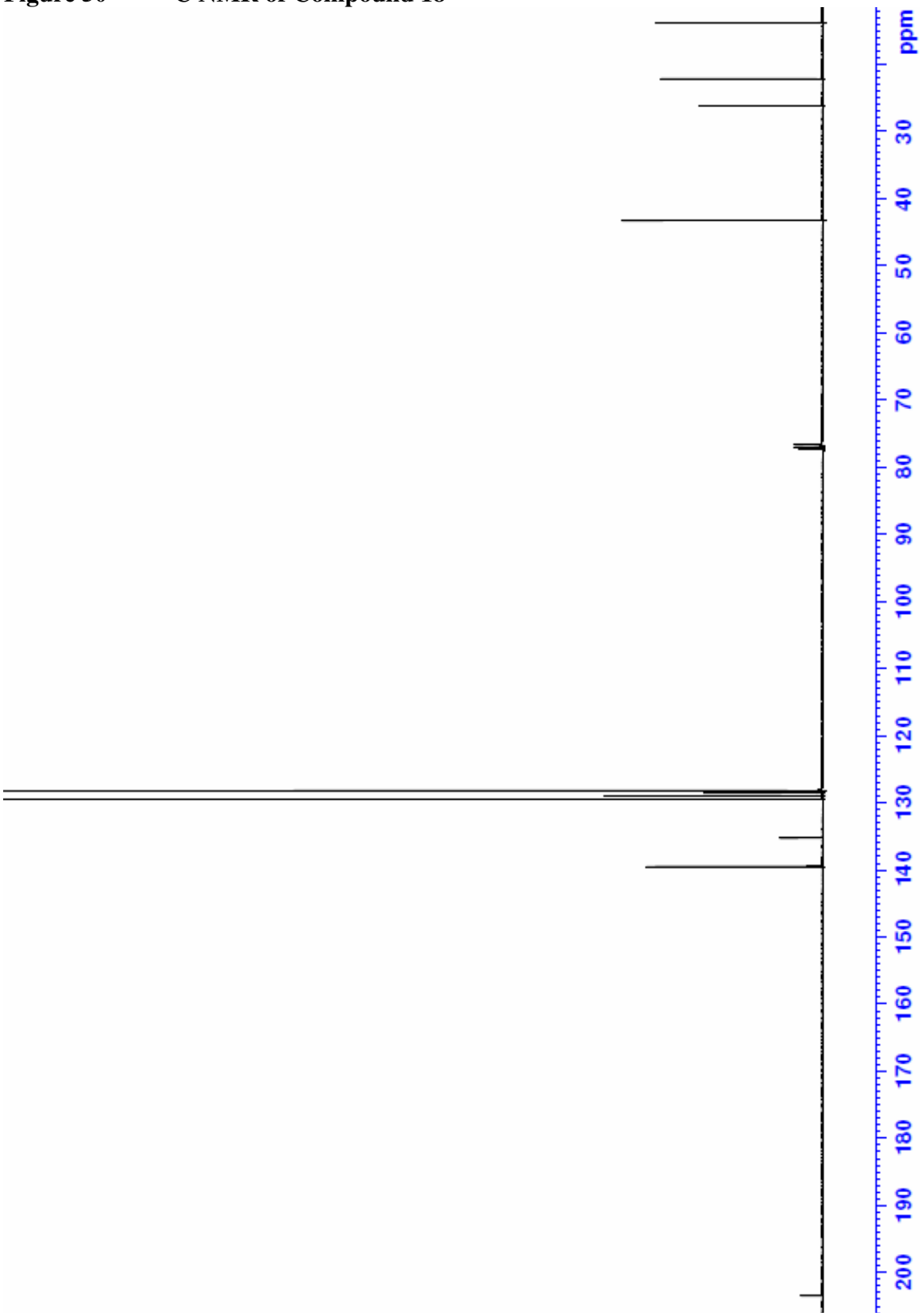


Figure 51 **^{1}H NMR of Compound 19**

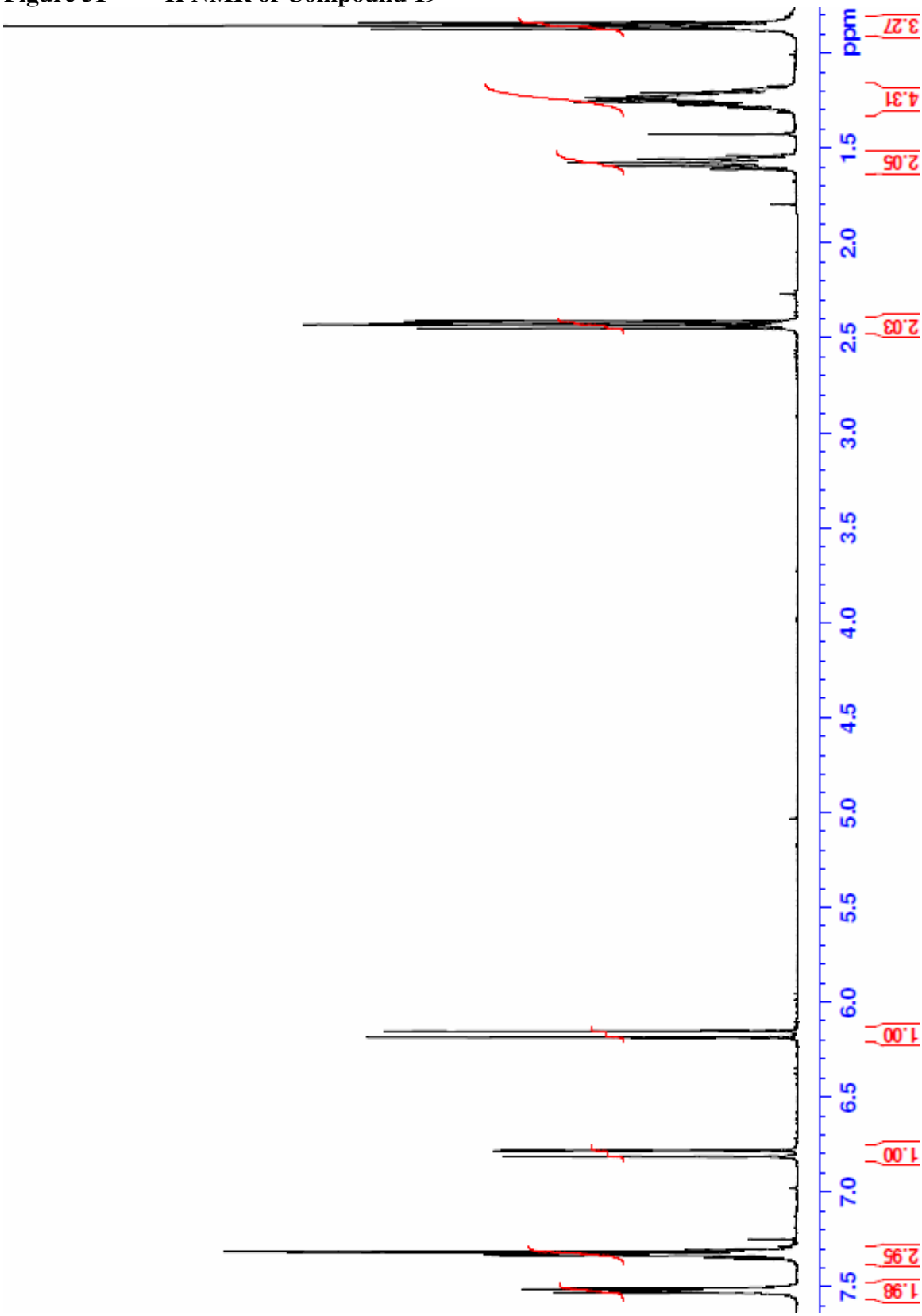


Figure 52 **^{13}C NMR of Compound 19**

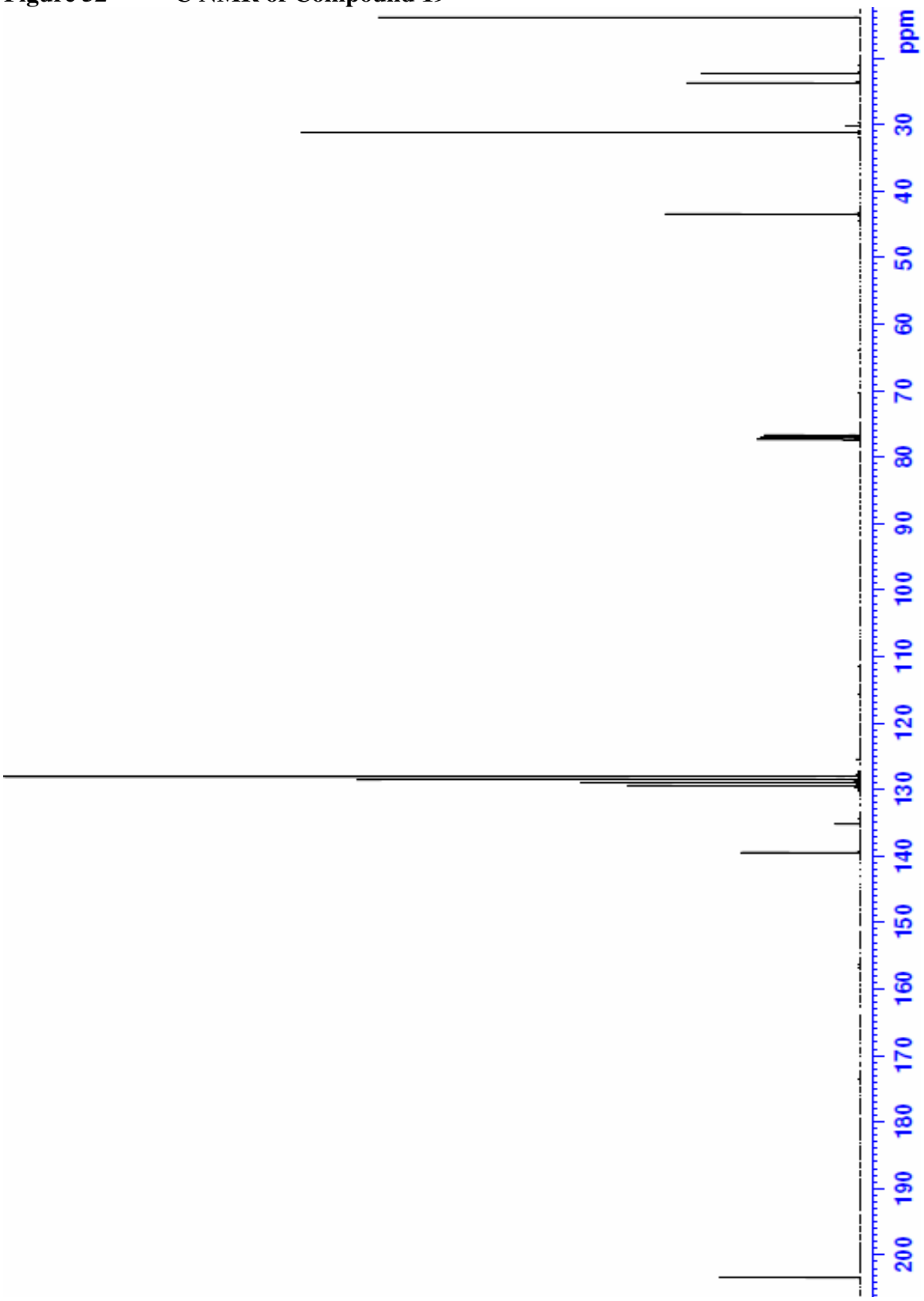


Figure 53 **^{1}H NMR of Compound 20**

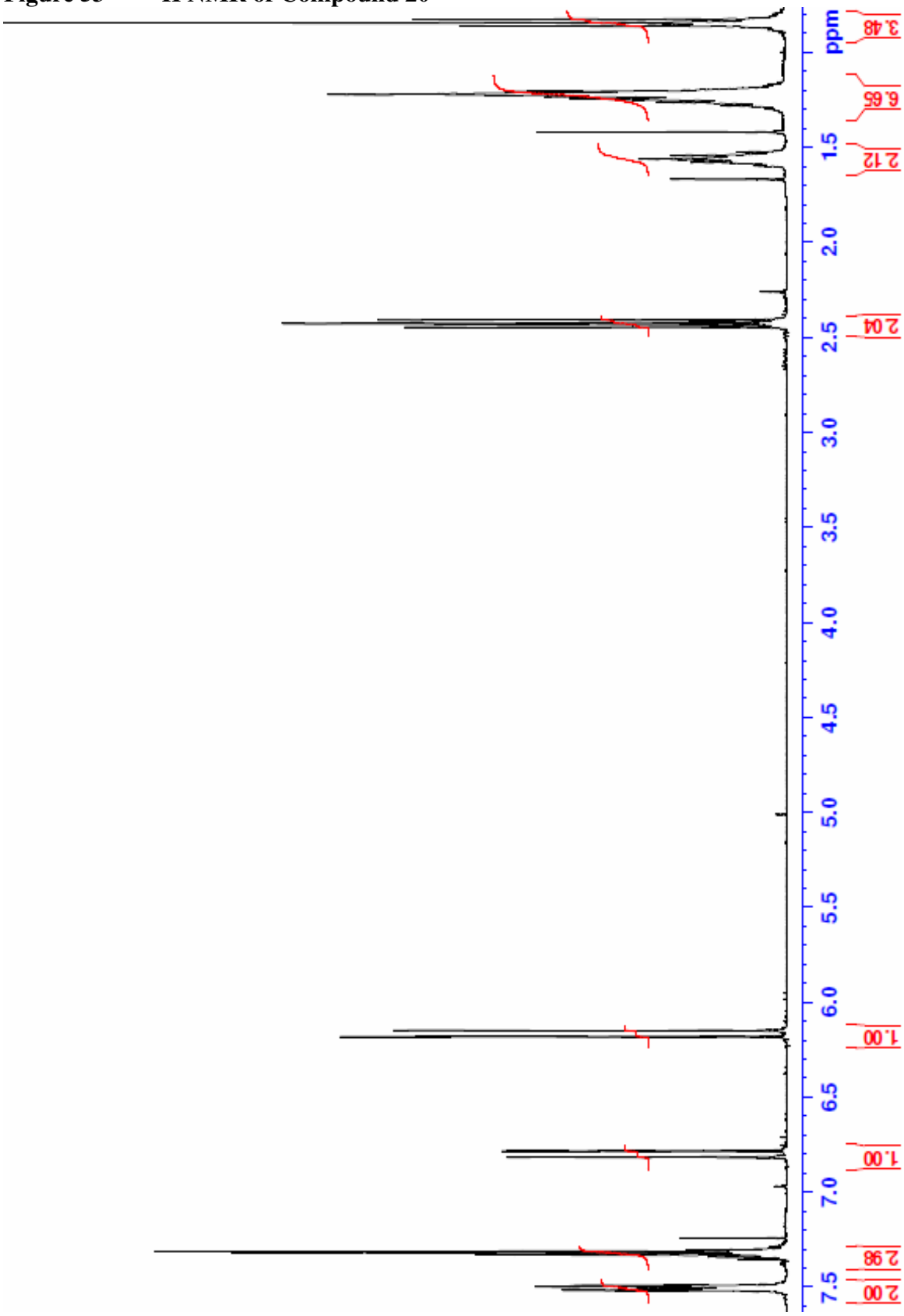


Figure 54 **^{13}C NMR of Compound 20**

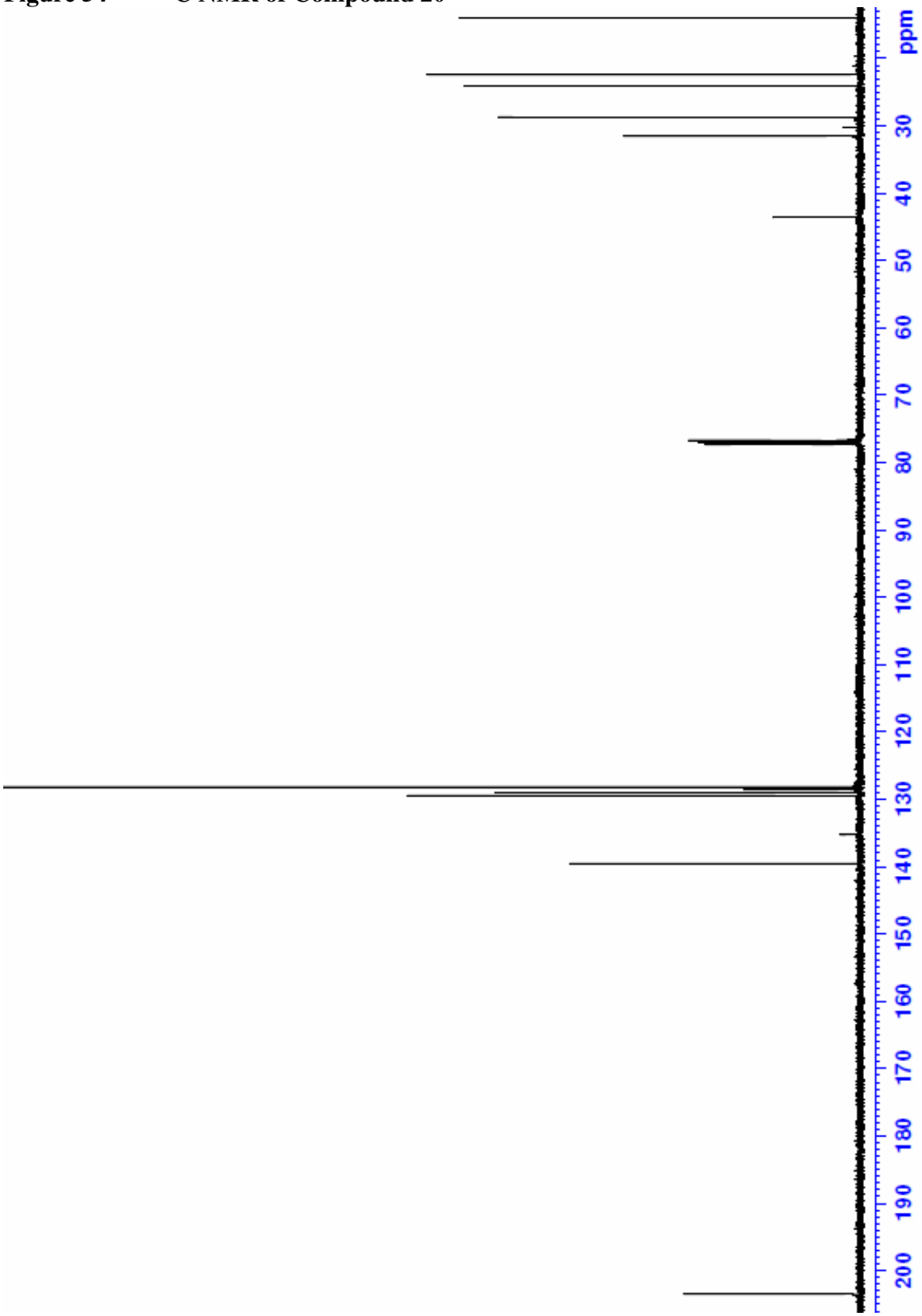


Figure 55 **^{1}H NMR of Compound 21**

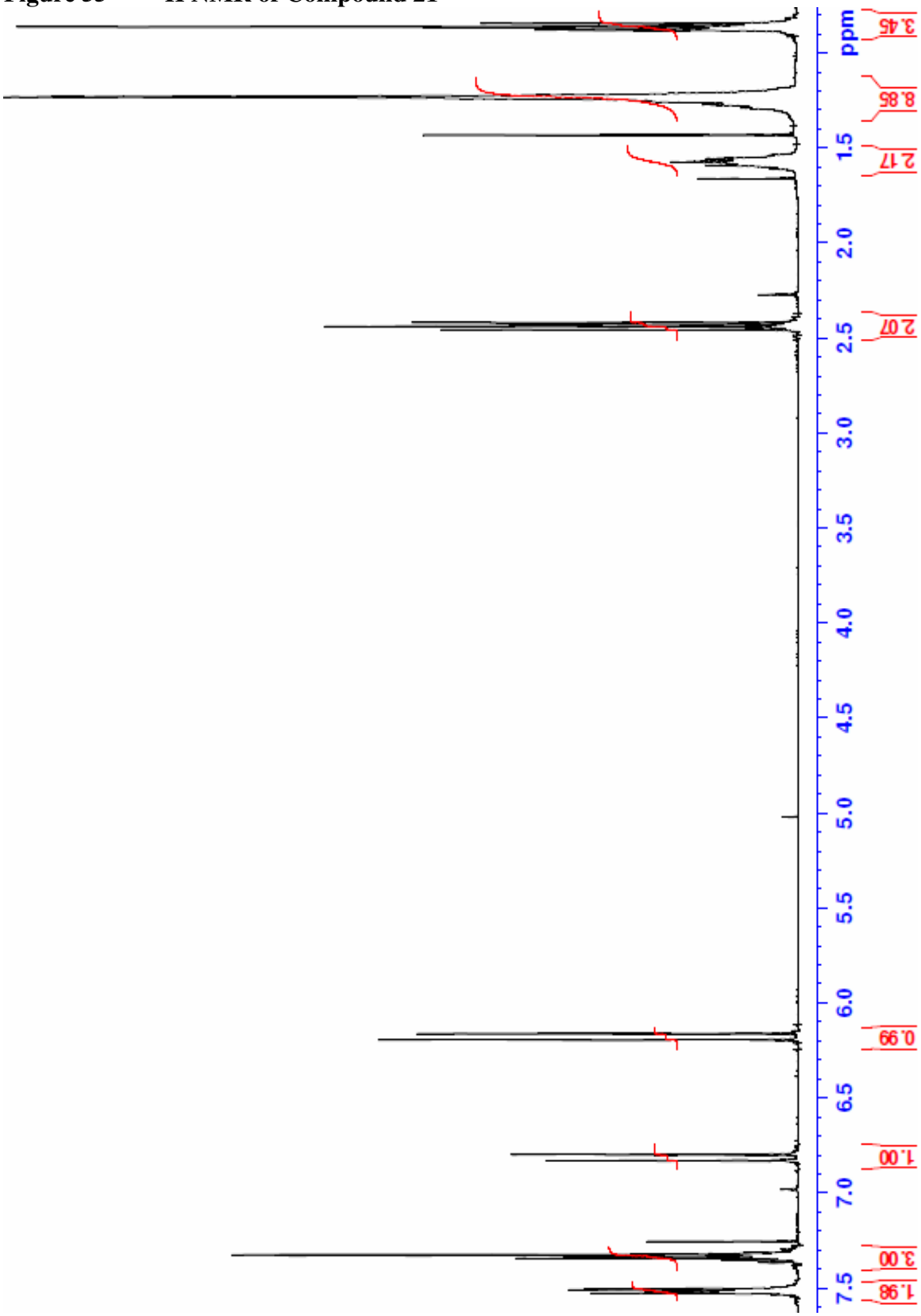


Figure 56 ^{13}C NMR of Compound 21

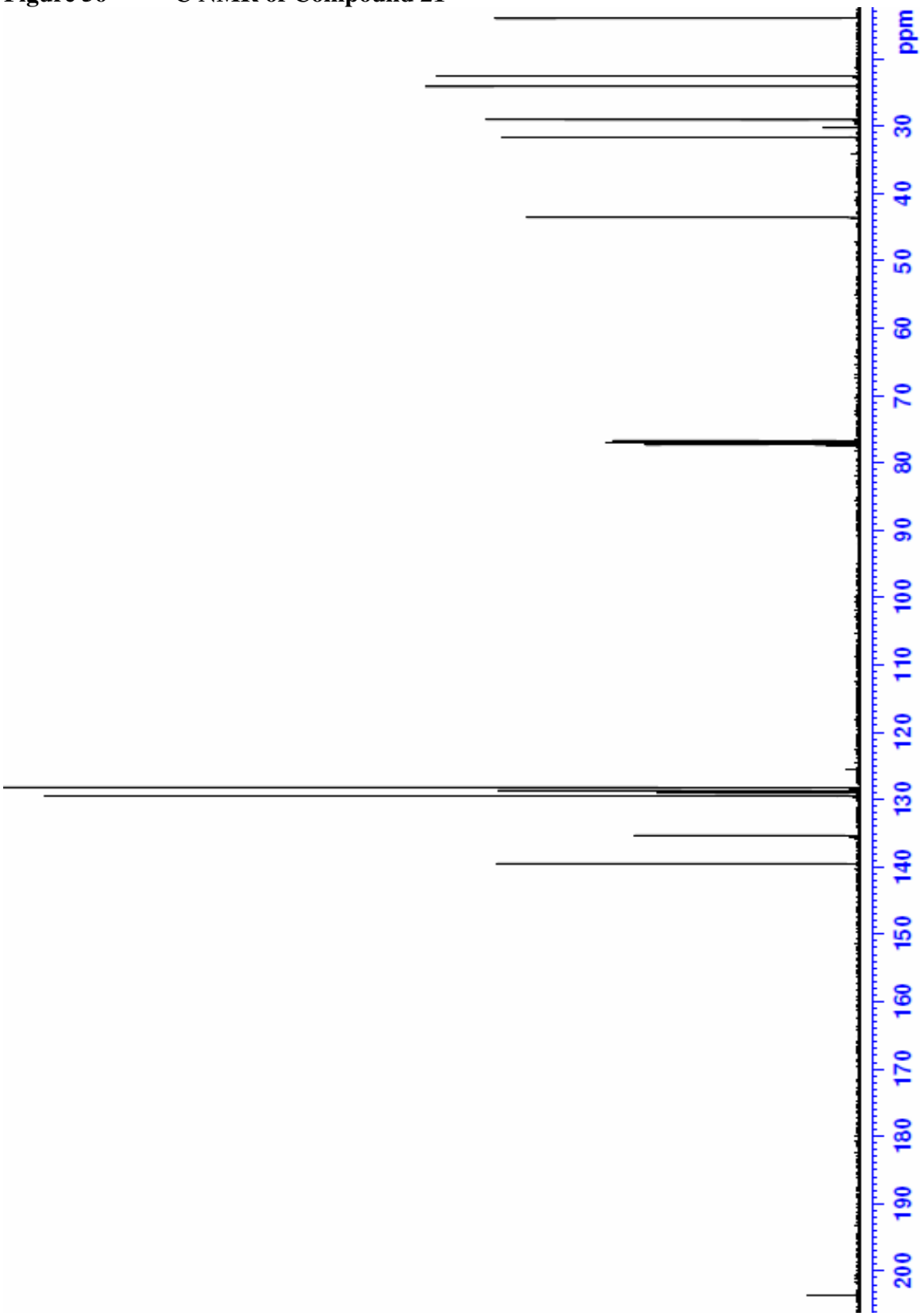


Figure 57 **^{1}H NMR of Compound 22**

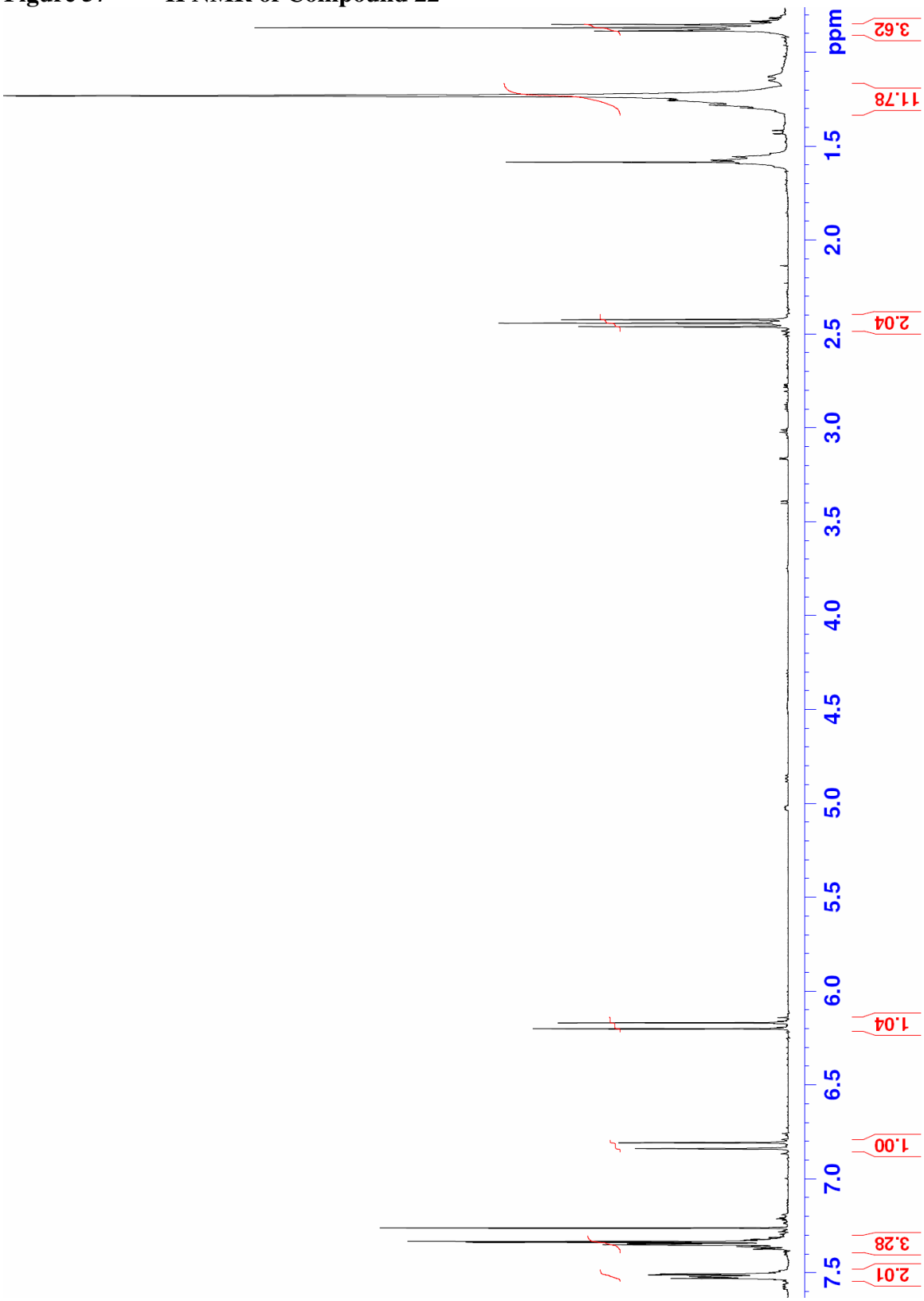
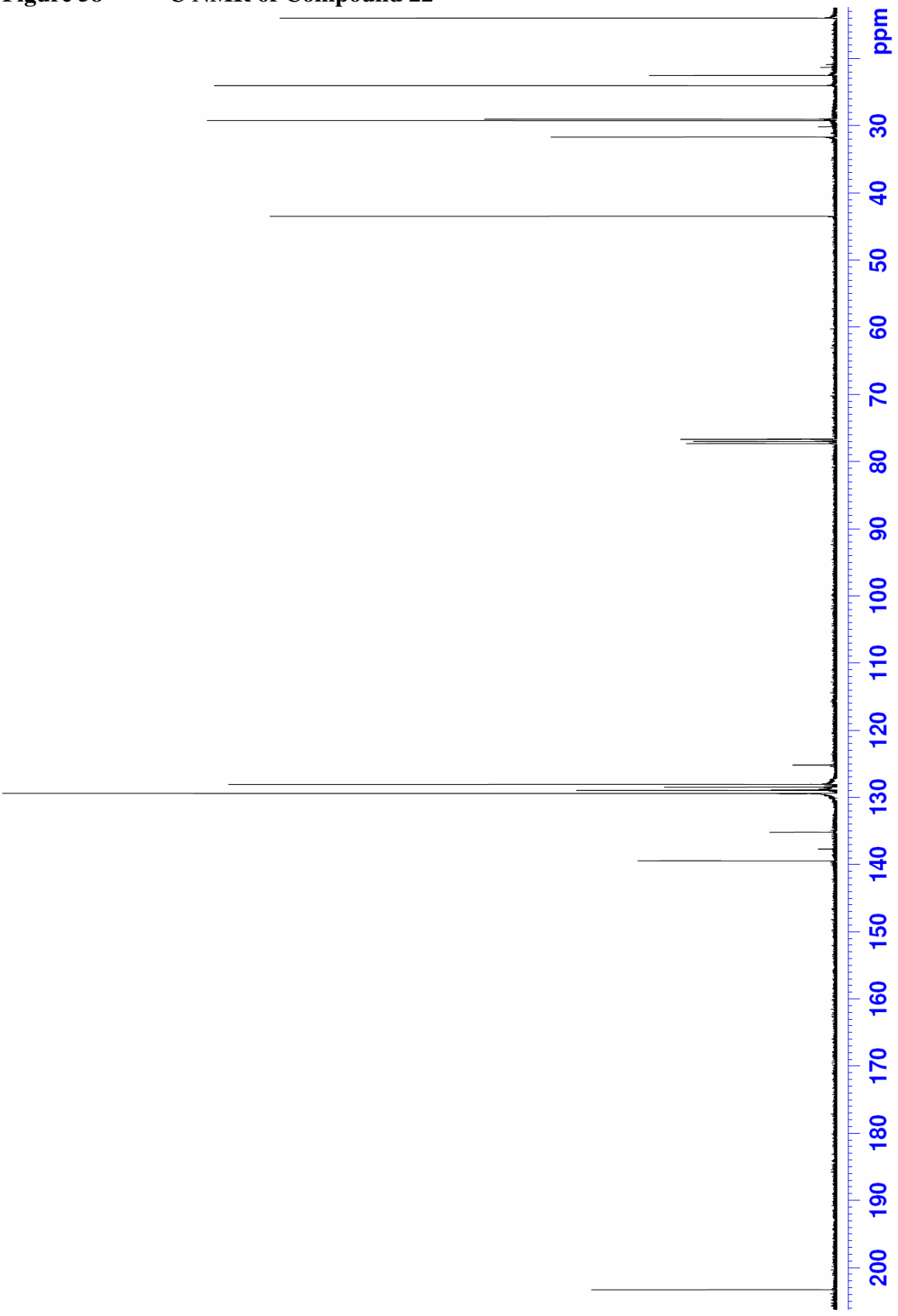
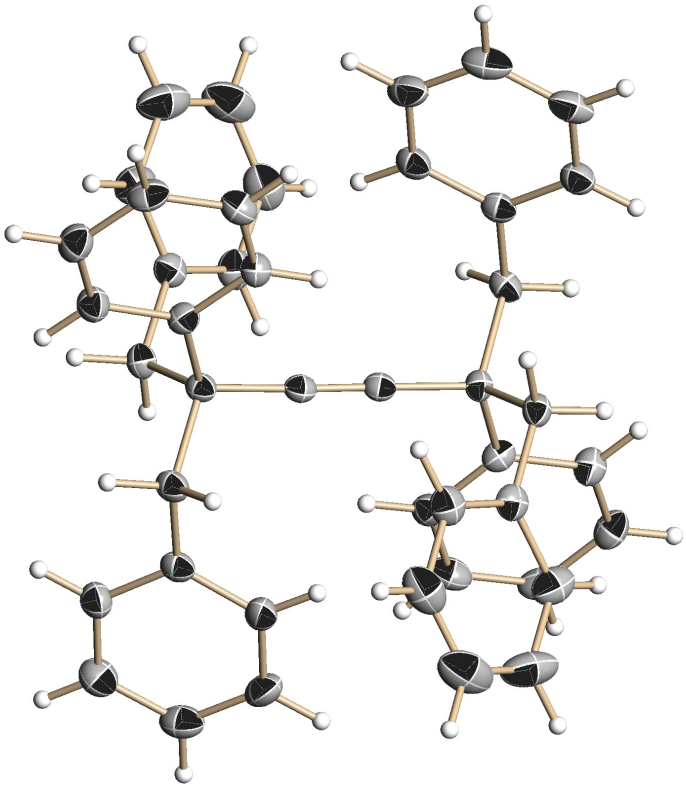


Figure 58 ^{13}C NMR of Compound 22



X-ray crystal structure data for 2,5-dibenzyl-1,2,5,6-tetraphenyl-3-hexyne



Data

Table 1. Crystal data and structure refinement for 07mz426m:

Identification code: 07mz426m
Empirical formula: C44 H38
Formula weight: 566.74
Temperature: 100(2) K
Wavelength: 0.71073 Å
Crystal system: Orthorhombic
Space group: $Pna2_1$
Unit cell dimensions:
a = 15.4917(12) Å, α = 90°
b = 12.2936(9) Å, β = 90°
c = 16.6974(13) Å, γ = 90°
Volume, *Z*: 3180.0(4) $Å^3$, 4

Density (calculated): 1.184 Mg/m^3
Absorption coefficient: 0.067 mm^{-1}
$F(000)$: 1208
Crystal size: 0.52 × 0.36 × 0.25 mm
Crystal shape, colour: block, colourless
θ range for data collection: 2.06 to 28.28°
Limiting indices: $-20 \leq h \leq 20$, $-16 \leq k \leq 12$, $-12 \leq l \leq 22$
Reflections collected: 16185
Independent reflections: 4083 (R(int) = 0.05620)
Completeness to θ = 28.28°: 99.9 %
Absorption correction: multi-scan
Max. and min. transmission: 0.983 and 0.824
Refinement method: Full-matrix least-squares on F^2
Data / restraints / parameters: 4083 / 1 / 397
Goodness-of-fit on F^2: 1.030
Final R indices [$I>2\sigma(I)$]: R1 = 0.0534, wR2 = 0.1211
R indices (all data): R1 = 0.0692, wR2 = 0.1314
Largest diff. peak and hole: 0.346 and −0.172 e × $Å^{-3}$

Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors

All hydrogen atoms were placed in calculated positions and all H atoms were refined with an isotropic displacement parameter 1.2 times that of the adjacent carbon atom.

Table 2. Atomic coordinates [× 10^4] and equivalent isotropic displacement parameters [$Å^2$ × 10^3] for 07mz426m. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	394(2)	6553(2)	82(2)	27(1)
C(2)	278(2)	7613(2)	−185(2)	29(1)

C(3)	501(2)	8481(2)	309(2)	31(1)
C(4)	835(2)	8274(3)	1057(2)	31(1)
C(5)	955(2)	7208(2)	1323(2)	26(1)
C(6)	735(2)	6339(2)	837(2)	22(1)
C(7)	843(2)	5144(2)	1109(2)	19(1)
C(8)	1183(2)	5085(2)	1931(2)	20(1)
C(9)	1430(2)	5015(2)	2602(2)	20(1)
C(10)	1776(2)	4929(2)	3423(2)	20(1)
C(11)	1858(2)	3728(2)	3686(2)	22(1)
C(12)	1578(2)	2877(2)	3204(2)	24(1)
C(13)	1657(2)	1798(2)	3452(2)	28(1)
C(14)	2009(2)	1569(2)	4197(2)	29(1)
C(15)	2287(2)	2406(2)	4682(2)	31(1)
C(16)	2210(2)	3477(2)	4431(2)	26(1)
C(17)	-40(2)	4535(2)	1097(2)	22(1)
C(18)	-699(2)	4969(2)	1681(2)	25(1)
C(19)	-1246(2)	5828(2)	1484(2)	35(1)
C(20)	-1849(2)	6203(3)	2032(3)	48(1)
C(21)	-1925(2)	5733(3)	2781(3)	51(1)
C(22)	-1391(2)	4879(3)	2985(2)	42(1)
C(23)	-782(2)	4495(2)	2439(2)	30(1)
C(24)	1499(2)	4584(2)	521(2)	23(1)
C(25)	1641(2)	3381(2)	643(2)	23(1)
C(26)	1181(2)	2625(2)	188(2)	27(1)
C(27)	1306(2)	1521(2)	304(2)	33(1)
C(28)	1889(2)	1147(2)	865(2)	36(1)
C(29)	2351(2)	1886(2)	1321(2)	32(1)
C(30)	2232(2)	3003(2)	1210(2)	25(1)
C(31)	1137(2)	5485(2)	4024(2)	24(1)
C(32)	979(2)	6691(2)	3927(2)	23(1)
C(33)	386(2)	7101(2)	3374(2)	28(1)
C(34)	221(2)	8203(3)	3322(2)	32(1)
C(35)	644(2)	8927(2)	3830(2)	34(1)
C(36)	1223(2)	8542(2)	4388(2)	33(1)
C(37)	1393(2)	7431(2)	4434(2)	28(1)
C(38)	2672(2)	5515(2)	3447(2)	23(1)
C(39)	3305(2)	5082(2)	2837(2)	24(1)
C(40)	3826(2)	4190(3)	2990(2)	34(1)
C(41)	4397(2)	3803(3)	2418(3)	46(1)
C(42)	4450(2)	4295(3)	1669(3)	48(1)
C(43)	3931(2)	5188(3)	1510(2)	39(1)
C(44)	3368(2)	5575(2)	2084(2)	30(1)

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell

esds is used for estimating esds involving l.s. planes.

Table 3. Bond lengths [Å] and angles [deg] for 07mz426m.

C(1)-C(2)	1.390(4)	C(23)-H(23)	0.9500
C(1)-C(6)	1.391(4)	C(24)-C(25)	1.509(4)
C(1)-H(1)	0.9500	C(24)-H(24A)	0.9900
C(2)-C(3)	1.392(5)	C(24)-H(24B)	0.9900
C(2)-H(2)	0.9500	C(25)-C(26)	1.396(4)
C(3)-C(4)	1.376(5)	C(25)-C(30)	1.398(4)
C(3)-H(3)	0.9500	C(26)-C(27)	1.384(4)
C(4)-C(5)	1.396(4)	C(26)-H(26)	0.9500
C(4)-H(4)	0.9500	C(27)-C(28)	1.381(5)
C(5)-C(6)	1.384(4)	C(27)-H(27)	0.9500
C(5)-H(5)	0.9500	C(28)-C(29)	1.385(5)
C(6)-C(7)	1.547(4)	C(28)-H(28)	0.9500
C(7)-C(8)	1.472(4)	C(29)-C(30)	1.397(4)
C(7)-C(17)	1.560(3)	C(29)-H(29)	0.9500
C(7)-C(24)	1.571(4)	C(30)-H(30)	0.9500
C(8)-C(9)	1.187(3)	C(31)-C(32)	1.511(4)
C(9)-C(10)	1.475(4)	C(31)-H(31A)	0.9900
C(10)-C(11)	1.546(4)	C(31)-H(31B)	0.9900
C(10)-C(38)	1.564(4)	C(32)-C(33)	1.398(4)
C(10)-C(31)	1.566(4)	C(32)-C(37)	1.399(4)
C(11)-C(12)	1.390(4)	C(33)-C(34)	1.381(4)
C(11)-C(16)	1.393(4)	C(33)-H(33)	0.9500
C(12)-C(13)	1.395(4)	C(34)-C(35)	1.394(5)
C(12)-H(12)	0.9500	C(34)-H(34)	0.9500
C(13)-C(14)	1.387(4)	C(35)-C(36)	1.378(4)
C(13)-H(13)	0.9500	C(35)-H(35)	0.9500
C(14)-C(15)	1.377(5)	C(36)-C(37)	1.392(4)
C(14)-H(14)	0.9500	C(36)-H(36)	0.9500
C(15)-C(16)	1.387(4)	C(37)-H(37)	0.9500
C(15)-H(15)	0.9500	C(38)-C(39)	1.510(4)
C(16)-H(16)	0.9500	C(38)-H(38A)	0.9900
C(17)-C(18)	1.510(4)	C(38)-H(38B)	0.9900
C(17)-H(17A)	0.9900	C(39)-C(40)	1.387(4)
C(17)-H(17B)	0.9900	C(39)-C(44)	1.399(4)
C(18)-C(19)	1.393(4)	C(40)-C(41)	1.386(5)
C(18)-C(23)	1.399(4)	C(40)-H(40)	0.9500
C(19)-C(20)	1.387(5)	C(41)-C(42)	1.392(6)
C(19)-H(19)	0.9500	C(41)-H(41)	0.9500
C(20)-C(21)	1.383(6)	C(42)-C(43)	1.386(5)
C(20)-H(20)	0.9500	C(42)-H(42)	0.9500
C(21)-C(22)	1.379(5)	C(43)-C(44)	1.381(4)
C(21)-H(21)	0.9500	C(43)-H(43)	0.9500
C(22)-C(23)	1.394(4)	C(44)-H(44)	0.9500
C(22)-H(22)	0.9500		

C(2)-C(1)-C(6) 121.2(3)
C(2)-C(1)-H(1) 119.4
C(6)-C(1)-H(1) 119.4
C(1)-C(2)-C(3) 119.7(3)
C(1)-C(2)-H(2) 120.1
C(3)-C(2)-H(2) 120.1
C(4)-C(3)-C(2) 119.4(3)
C(4)-C(3)-H(3) 120.3
C(2)-C(3)-H(3) 120.3
C(3)-C(4)-C(5) 120.8(3)
C(3)-C(4)-H(4) 119.6
C(5)-C(4)-H(4) 119.6
C(6)-C(5)-C(4) 120.4(3)
C(6)-C(5)-H(5) 119.8
C(4)-C(5)-H(5) 119.8
C(5)-C(6)-C(1) 118.6(3)
C(5)-C(6)-C(7) 122.3(3)
C(1)-C(6)-C(7) 119.1(2)
C(8)-C(7)-C(6) 111.1(2)
C(8)-C(7)-C(17) 107.6(2)
C(6)-C(7)-C(17) 110.9(2)
C(8)-C(7)-C(24) 109.3(2)
C(6)-C(7)-C(24) 107.6(2)
C(17)-C(7)-C(24) 110.4(2)
C(9)-C(8)-C(7) 177.6(3)
C(8)-C(9)-C(10) 177.5(3)
C(9)-C(10)-C(11) 111.2(2)
C(9)-C(10)-C(38) 108.3(2)
C(11)-C(10)-C(38) 111.1(2)
C(9)-C(10)-C(31) 109.5(2)
C(11)-C(10)-C(31) 106.7(2)
C(38)-C(10)-C(31) 110.1(2)
C(12)-C(11)-C(16) 118.2(3)
C(12)-C(11)-C(10) 122.0(2)
C(16)-C(11)-C(10) 119.8(2)
C(11)-C(12)-C(13) 121.1(3)
C(11)-C(12)-H(12) 119.4
C(13)-C(12)-H(12) 119.4
C(14)-C(13)-C(12) 119.5(3)
C(14)-C(13)-H(13) 120.2
C(12)-C(13)-H(13) 120.2
C(15)-C(14)-C(13) 119.9(3)
C(15)-C(14)-H(14) 120.0
C(13)-C(14)-H(14) 120.0
C(14)-C(15)-C(16) 120.3(3)
C(14)-C(15)-H(15) 119.9
C(16)-C(15)-H(15) 119.9
C(15)-C(16)-C(11) 120.9(3)
C(15)-C(16)-H(16) 119.5
C(11)-C(16)-H(16) 119.5
C(18)-C(17)-C(7) 114.5(2)
C(18)-C(17)-H(17A) 108.6
C(7)-C(17)-H(17A) 108.6
C(18)-C(17)-H(17B) 108.6
C(7)-C(17)-H(17B) 108.6
H(17A)-C(17)-H(17B) 107.6
C(19)-C(18)-C(23) 118.3(3)
C(19)-C(18)-C(17) 121.8(3)
C(23)-C(18)-C(17) 120.0(3)
C(20)-C(19)-C(18) 120.4(3)
C(20)-C(19)-H(19) 119.8
C(18)-C(19)-H(19) 119.8
C(21)-C(20)-C(19) 121.1(3)
C(21)-C(20)-H(20) 119.5
C(19)-C(20)-H(20) 119.5
C(22)-C(21)-C(20) 119.3(3)
C(22)-C(21)-H(21) 120.4
C(20)-C(21)-H(21) 120.4
C(21)-C(22)-C(23) 120.2(3)
C(21)-C(22)-H(22) 119.9
C(23)-C(22)-H(22) 119.9
C(22)-C(23)-C(18) 120.8(3)
C(22)-C(23)-H(23) 119.6
C(18)-C(23)-H(23) 119.6
C(25)-C(24)-C(7) 116.1(2)
C(25)-C(24)-H(24A) 108.3
C(7)-C(24)-H(24A) 108.3
C(25)-C(24)-H(24B) 108.3
C(7)-C(24)-H(24B) 108.3
H(24A)-C(24)-H(24B) 107.4
C(26)-C(25)-C(30) 118.8(3)
C(26)-C(25)-C(24) 120.4(3)
C(30)-C(25)-C(24) 120.9(2)
C(27)-C(26)-C(25) 120.4(3)
C(27)-C(26)-H(26) 119.8

C(25)-C(26)-H(26)	119.8
C(28)-C(27)-C(26)	120.8(3)
C(28)-C(27)-H(27)	119.6
C(26)-C(27)-H(27)	119.6
C(27)-C(28)-C(29)	119.5(3)
C(27)-C(28)-H(28)	120.2
C(29)-C(28)-H(28)	120.2
C(28)-C(29)-C(30)	120.3(3)
C(28)-C(29)-H(29)	119.9
C(30)-C(29)-H(29)	119.9
C(29)-C(30)-C(25)	120.2(3)
C(29)-C(30)-H(30)	119.9
C(25)-C(30)-H(30)	119.9
C(32)-C(31)-C(10)	117.5(2)
C(32)-C(31)-H(31A)	107.9
C(10)-C(31)-H(31A)	107.9
C(32)-C(31)-H(31B)	107.9
C(10)-C(31)-H(31B)	107.9
H(31A)-C(31)-H(31B)	107.2
C(33)-C(32)-C(37)	117.8(3)
C(33)-C(32)-C(31)	122.0(3)
C(37)-C(32)-C(31)	120.0(3)
C(34)-C(33)-C(32)	121.1(3)
C(34)-C(33)-H(33)	119.4
C(32)-C(33)-H(33)	119.4
C(33)-C(34)-C(35)	120.1(3)
C(33)-C(34)-H(34)	120.0
C(35)-C(34)-H(34)	120.0
C(36)-C(35)-C(34)	119.9(3)
C(36)-C(35)-H(35)	120.0
C(34)-C(35)-H(35)	120.0
C(35)-C(36)-C(37)	119.9(3)
C(35)-C(36)-H(36)	120.1
C(37)-C(36)-H(36)	120.1
C(36)-C(37)-C(32)	121.2(3)
C(36)-C(37)-H(37)	119.4
C(32)-C(37)-H(37)	119.4
C(39)-C(38)-C(10)	113.4(2)
C(39)-C(38)-H(38A)	108.9
C(10)-C(38)-H(38A)	108.9
C(39)-C(38)-H(38B)	108.9
C(10)-C(38)-H(38B)	108.9
H(38A)-C(38)-H(38B)	107.7
C(40)-C(39)-C(44)	117.9(3)
C(40)-C(39)-C(38)	122.2(3)
C(44)-C(39)-C(38)	120.0(3)
C(41)-C(40)-C(39)	121.1(3)
C(41)-C(40)-H(40)	119.5
C(39)-C(40)-H(40)	119.5
C(40)-C(41)-C(42)	120.5(3)
C(40)-C(41)-H(41)	119.7
C(42)-C(41)-H(41)	119.7
C(43)-C(42)-C(41)	118.8(3)
C(43)-C(42)-H(42)	120.6
C(41)-C(42)-H(42)	120.6
C(44)-C(43)-C(42)	120.4(3)
C(44)-C(43)-H(43)	119.8
C(42)-C(43)-H(43)	119.8
C(43)-C(44)-C(39)	121.2(3)
C(43)-C(44)-H(44)	119.4
C(39)-C(44)-H(44)	119.4

Table 4. Anisotropic displacement parameters [$Å^2 \times 10^3$] for 07mz426m. The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [(h a*)^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	28(1)	25(1)	28(2)	3(1)	-4(1)	-5(1)
C(2)	27(2)	33(2)	27(2)	10(1)	-2(1)	0(1)
C(3)	34(2)	20(1)	40(2)	9(1)	7(1)	5(1)
C(4)	35(2)	23(2)	36(2)	-6(1)	7(1)	-1(1)
C(5)	25(1)	29(2)	24(1)	0(1)	3(1)	3(1)
C(6)	20(1)	21(1)	25(1)	4(1)	1(1)	-1(1)
C(7)	21(1)	19(1)	18(1)	1(1)	-2(1)	-2(1)
C(8)	22(1)	16(1)	23(1)	0(1)	1(1)	0(1)
C(9)	20(1)	18(1)	24(1)	-2(1)	2(1)	0(1)
C(10)	22(1)	18(1)	20(1)	0(1)	1(1)	1(1)
C(11)	22(1)	24(1)	21(1)	3(1)	1(1)	0(1)
C(12)	24(1)	25(2)	22(1)	0(1)	-2(1)	-1(1)
C(13)	31(2)	25(2)	28(2)	-3(1)	4(1)	-2(1)
C(14)	32(2)	21(1)	35(2)	7(1)	3(1)	5(1)
C(15)	32(2)	34(2)	27(2)	5(1)	-2(1)	2(1)
C(16)	30(2)	26(1)	24(1)	1(1)	-2(1)	0(1)
C(17)	25(1)	19(1)	23(1)	0(1)	-5(1)	-2(1)
C(18)	23(1)	23(1)	29(2)	-1(1)	-2(1)	-7(1)
C(19)	26(2)	28(2)	49(2)	3(1)	-2(1)	-3(1)
C(20)	28(2)	33(2)	85(3)	-5(2)	7(2)	3(1)
C(21)	33(2)	54(2)	66(3)	-20(2)	19(2)	-12(2)
C(22)	35(2)	55(2)	36(2)	-10(2)	11(2)	-17(2)
C(23)	26(1)	33(2)	30(2)	-1(1)	0(1)	-7(1)
C(24)	28(1)	21(1)	20(1)	-1(1)	3(1)	-2(1)
C(25)	24(1)	23(1)	22(1)	-1(1)	6(1)	1(1)
C(26)	27(1)	29(2)	25(2)	-4(1)	3(1)	2(1)
C(27)	30(2)	28(2)	41(2)	-10(1)	12(1)	-3(1)
C(28)	41(2)	24(2)	42(2)	1(1)	16(2)	3(1)
C(29)	37(2)	33(2)	26(2)	3(1)	7(1)	11(1)
C(30)	29(1)	26(1)	20(1)	-1(1)	5(1)	1(1)
C(31)	29(1)	24(1)	19(1)	1(1)	4(1)	2(1)
C(32)	25(1)	24(1)	21(1)	0(1)	6(1)	1(1)
C(33)	24(1)	38(2)	23(1)	-4(1)	0(1)	5(1)
C(34)	31(2)	38(2)	29(2)	6(1)	-1(1)	13(1)
C(35)	40(2)	25(2)	37(2)	2(1)	7(1)	7(1)
C(36)	37(2)	28(2)	35(2)	-4(1)	0(1)	-3(1)
C(37)	31(2)	29(2)	23(2)	-1(1)	-2(1)	0(1)
C(38)	24(1)	24(1)	22(1)	-1(1)	-2(1)	-4(1)
C(39)	21(1)	25(1)	28(2)	-4(1)	0(1)	-6(1)
C(40)	28(2)	33(2)	41(2)	3(1)	1(1)	-2(1)
C(41)	29(2)	37(2)	74(3)	-6(2)	5(2)	2(1)

C(42)	33(2)	57(2)	56(2)	−16(2)	19(2)	−6(2)
C(43)	31(2)	53(2)	34(2)	−4(2)	8(1)	−13(2)
C(44)	25(1)	32(2)	32(2)	0(1)	−2(1)	−7(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for 07mz426m.

	x	y	z	U(eq)
H(1)	238	5963	−256	32
H(2)	47	7746	−703	35
H(3)	422	9208	132	37
H(4)	986	8864	1397	38
H(5)	1189	7078	1840	31
H(12)	1328	3032	2697	28
H(13)	1470	1223	3114	34
H(14)	2059	837	4372	35
H(15)	2532	2248	5190	37
H(16)	2400	4047	4772	32
H(17A)	−283	4579	549	27
H(17B)	63	3757	1217	27
H(19)	−1205	6159	971	41
H(20)	−2216	6792	1891	58
H(21)	−2341	5995	3152	61
H(22)	−1439	4551	3498	50
H(23)	−420	3903	2583	35
H(24A)	1293	4700	−33	28
H(24B)	2062	4957	572	28
H(26)	780	2869	−203	32
H(27)	986	1015	−7	39
H(28)	1973	387	938	43
H(29)	2750	1633	1710	38
H(30)	2554	3506	1522	30
H(31A)	574	5109	3981	29
H(31B)	1356	5359	4573	29
H(33)	90	6613	3028	34
H(34)	−181	8468	2939	39
H(35)	533	9685	3792	41
H(36)	1506	9033	4740	40
H(37)	1798	7172	4817	33
H(38A)	2585	6302	3351	28
H(38B)	2924	5430	3988	28
H(40)	3792	3838	3496	41
H(41)	4755	3197	2538	55
H(42)	4834	4024	1273	58
H(43)	3963	5536	1003	47
H(44)	3017	6188	1966	36

Table 6. Torsion angles [deg] for 07mz426m

C(6)-C(1)-C(2)-C(3)	-0.4(4)
C(1)-C(2)-C(3)-C(4)	0.1(4)
C(2)-C(3)-C(4)-C(5)	0.2(5)
C(3)-C(4)-C(5)-C(6)	-0.3(4)
• C(4)-C(5)-C(6)-C(1)	0.1(4)
• C(4)-C(5)-C(6)-C(7)	-179.1(2)
• C(2)-C(1)-C(6)-C(5)	0.3(4)
• C(2)-C(1)-C(6)-C(7)	179.4(3)
• C(5)-C(6)-C(7)-C(8)	1.2(4)
• C(1)-C(6)-C(7)-C(8)	-177.9(2)
C(5)-C(6)-C(7)-C(17)	120.8(3)
C(1)-C(6)-C(7)-C(17)	-58.4(3)
C(5)-C(6)-C(7)-C(24)	-118.4(3)
C(1)-C(6)-C(7)-C(24)	62.5(3)
C(9)-C(10)-C(11)-C(12)	-3.9(4)
C(38)-C(10)-C(11)-C(12)	-124.5(3)
C(31)-C(10)-C(11)-C(12)	115.5(3)
C(9)-C(10)-C(11)-C(16)	177.1(2)
C(38)-C(10)-C(11)-C(16)	56.5(3)
C(31)-C(10)-C(11)-C(16)	-63.5(3)
C(16)-C(11)-C(12)-C(13)	-0.9(4)
C(10)-C(11)-C(12)-C(13)	-179.9(2)
C(11)-C(12)-C(13)-C(14)	0.9(4)
C(12)-C(13)-C(14)-C(15)	-0.7(4)
C(13)-C(14)-C(15)-C(16)	0.4(5)
C(14)-C(15)-C(16)-C(11)	-0.4(5)
C(12)-C(11)-C(16)-C(15)	0.7(4)
C(10)-C(11)-C(16)-C(15)	179.7(3)
C(8)-C(7)-C(17)-C(18)	57.3(3)
C(6)-C(7)-C(17)-C(18)	-64.4(3)
C(24)-C(7)-C(17)-C(18)	176.4(2)
C(7)-C(17)-C(18)-C(19)	86.6(3)
C(7)-C(17)-C(18)-C(23)	-94.5(3)
C(23)-C(18)-C(19)-C(20)	0.6(4)
C(17)-C(18)-C(19)-C(20)	179.5(3)
C(18)-C(19)-C(20)-C(21)	-0.4(5)
C(19)-C(20)-C(21)-C(22)	0.1(5)
C(20)-C(21)-C(22)-C(23)	-0.1(5)
C(21)-C(22)-C(23)-C(18)	0.4(5)
C(19)-C(18)-C(23)-C(22)	-0.6(4)
C(17)-C(18)-C(23)-C(22)	-179.5(3)
C(8)-C(7)-C(24)-C(25)	64.0(3)
C(6)-C(7)-C(24)-C(25)	-175.3(2)
C(17)-C(7)-C(24)-C(25)	-54.1(3)
C(7)-C(24)-C(25)-C(26)	95.9(3)
C(7)-C(24)-C(25)-C(30)	-84.0(3)
C(30)-C(25)-C(26)-C(27)	0.5(4)
C(24)-C(25)-C(26)-C(27)	-179.5(2)
C(25)-C(26)-C(27)-C(28)	-0.4(4)

C(26)-C(27)-C(28)-C(29)	0.4(4)
C(27)-C(28)-C(29)-C(30)	-0.4(4)
C(28)-C(29)-C(30)-C(25)	0.5(4)
C(26)-C(25)-C(30)-C(29)	-0.5(4)
C(24)-C(25)-C(30)-C(29)	179.4(2)
C(9)-C(10)-C(31)-C(32)	-62.8(3)
C(11)-C(10)-C(31)-C(32)	176.7(2)
C(38)-C(10)-C(31)-C(32)	56.1(3)
C(10)-C(31)-C(32)-C(33)	82.7(3)
C(10)-C(31)-C(32)-C(37)	-101.3(3)
C(37)-C(32)-C(33)-C(34)	0.9(4)
C(31)-C(32)-C(33)-C(34)	176.9(3)
C(32)-C(33)-C(34)-C(35)	-0.6(4)
C(33)-C(34)-C(35)-C(36)	-0.3(5)
C(34)-C(35)-C(36)-C(37)	0.9(5)
C(35)-C(36)-C(37)-C(32)	-0.6(5)
C(33)-C(32)-C(37)-C(36)	-0.3(4)
C(31)-C(32)-C(37)-C(36)	-176.4(3)
C(9)-C(10)-C(38)-C(39)	-55.8(3)
C(11)-C(10)-C(38)-C(39)	66.6(3)
C(31)-C(10)-C(38)-C(39)	-175.5(2)
C(10)-C(38)-C(39)-C(40)	-86.1(3)
C(10)-C(38)-C(39)-C(44)	92.9(3)
C(44)-C(39)-C(40)-C(41)	0.4(4)
C(38)-C(39)-C(40)-C(41)	179.5(3)
C(39)-C(40)-C(41)-C(42)	-0.9(5)
C(40)-C(41)-C(42)-C(43)	0.9(5)
C(41)-C(42)-C(43)-C(44)	-0.5(5)
C(42)-C(43)-C(44)-C(39)	0.0(5)
C(40)-C(39)-C(44)-C(43)	0.0(4)
C(38)-C(39)-C(44)-C(43)	-179.0(3)